ASSOCIATION BETWEEN RADIATION DOSE TO THE PHARYNGEAL CONSTRICTORS AND SWALLOWING DYSFUNCTION AND PATIENTS QUALITY OF LIFE FOLLOWING RADIOTHERAPY OR CHEMORADIOTHERAPY FOR HEAD AND NECK CANCERS

DEPARTMENT OF RADIOTHERAPY

CHRISTIAN MEDICAL COLLEGE

VELLORE 632004

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF

MD BRANCH IX RADIOTHERAPY

EXAMINATION APRIL 2016

TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY

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CERTIFICATE

This is to certify that the dissertation entitled "ASSOCIATION BETWEEN THE RADIATION DOSES TO THE PHARYNGEAL CONSTRICTORS AND SWALLOWING DYSFUNCTION AND PATIENTS QUALITY OF LIFE FOLLOWING RADIOTHERAPY OR CHEMORADIOTHERAPY " is a bonafide work done by Dr. SANTANU SAMANTA, Post Graduate Student in the Department of Radiotherapy, Christian Medical College, Vellore during the period from April 2014 to April 2016 and is being submitted to The Tamil Nadu Dr. M. G. R Medical University in partial fulfilment of the MD Branch IX Radiotherapy examination conducted in April 2016.

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I, Santanu Samanta, PG Registrar, Department of Radiation therapy, Christian Medical College Vellore hereby declare that the dissertation titled 'ASSOCIATION BETWEEN THE RADIATION DOSES TO THE PHARYNGEAL CONSTRICTORS AND SWALLOWING DYSFUNCTION AND PATIENTS QUALITY OF LIFE FOLLOWING RADIOTHERAPY OR CHEMO RADIOTHERAPY ' is a bonafide work done by me for partial fulfilment towards MD Radiotherapy (Branch IX) Degree examination of the Tamil Nadu Dr M G R Medical University to be held in April 2016.

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Dear Dr. Santanu Samanta ,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed the following amendments for the study titled: "Association between the radiation dose to the pharyngeal constrictors and swallowing dysfunction and patients quality of life following chemo irradiation for head and neck cancers"

1. Patients diagnosed to have biopsy proven malignancy of the head and neck Aged 18 years or older.
2. Planned for radical radiotherapy with or without chemotherapy (Weekly/three weekly).
3. Planned for post operative radiotherapy with or without chemotherapy (weekly/three weekly).
4. Radiation therapy with intensity modulated radiation therapy (IMRT).
5. Willing for evaluation of their swallowing function using FEES.
6. No baseline swallowing dysfunction/Radiologically no evidence of disease in the pharyngeal constrictors.

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on March 03rd 2015 at 12.45 pm in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Other Affiliations
Dr. Iriah Samuvam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician

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Dr. Rajesh Kannangai	MD, Ph D.	Professor & In-charge Retrovirus Laboratory (NRL under NACO), Department of Clinical Virology, CMC, Vellore	Internal, Clinician
Dr. Niranjan Thomas	DCH, MD, DNB (Paediatrics)	Professor, Neonatology, CMC, Vellore	Internal, Clinician
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We approve the above amendments as presented.

Yours sincerely,

Dr. B. J. Prashantham
Chairperson (Ethics Committee)
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Cc: Dr. Subhashini John, Radiation Therapy Unit - II, CMC, Vellore

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Mr. Robby Pria Sundersingh
The Treasurer
Christian Medical College,
Vellore.

Dear Mr. Robby Pria Sundersingh,

Sub: **Fluid Research Grant Project:**
Association between the radiation doses to the pharyngeal constrictors and swallowing dysfunction and patients' quality of life following chemo irradiation for head and neck cancers.
Dr. Santanu Samanta, PG Registrar, Dr. Subhashini John, Dr. Rajesh Isiah, Dr. Saikat Das, Radiation Therapy, Dr. Anand Job, ENT, Dr. Rajiv C. Michael, Dr. Rajan Sundaresan, Dr. Rita Ruby Anbuselvi, Dr. Suma Susan Mathews, Mr. Timothy Peace, Radiation Therapy,Dr. Swapna Sebastian, Mrs. Shipra Chrysollete, ENT, CMC, Vellore.

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The Institutional Review Board at its meeting held on April 7th 2014 vide IRB Min. No. **8827** accepted the project *for a total 10,000/- INR (Rupees Ten Thousand only) will be granted for 6 months with the* ***Account Head: 22Y369****. There has been a change of* ***Principal Investigator from Dr. Mayur Mayank to Dr.*** **Santanu Samanta**, Radiation Therapy, CMC, Vellore. On account of which kindly make arrangement for the account to be operated Dr. Santanu Samanta (docsantanu@gmail.com & drsantanu@cmcvellore.ac.in) and Dr. Subhashini John (subha@cmcvellore.ac.in)

Yours sincerely,

B. J. Prashantham

Dr. B. J. Prashantham
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INTRODUCTION

Head and neck cancers are a major cause of morbidity and mortality throughout the world. In India the incidence of head and neck cancers are very high and it is the third most commonly diagnosed malignancy after breast and cervical cancers[1-3]. Management of early stage head and neck cancers requires a single modality where as multi modality approach is essential for advanced stage head and neck cancers.

Radiation therapy which is an important modality in cancer treatment particularly in head and neck cancer has gone through significant evolution. It started with conventional radiotherapy using the Cobalt therapy unit and has evolved to conformal therapy using Linear Accelerator with 3Dimensional Conformal Radiation Therapy (3DCRT) and Intensity Modulated Radiation Therapy (IMRT). IMRT has become the standard of care in delivering radiation therapy for head and neck cancers as it helps to maximize dose to normal structures close to the target site, with less escalation in the tumour at the same time [4,5].

Head and neck cancers treated with radiation therapy can cause significant morbidity post treatment in the form of mucositis, xerostomia and dysphagia. Although IMRT can help in reducing dose to the salivary glands and reduce xerostomia and dysphagia, its role in preventing dysphagia by reducing dose to pharyngeal structures and cricopharyngeal muscles is controversial.

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Contents

ABSTRACT TITLE: ASSOCIATION BETWEEN THE RADIATION DOSES TO THE PHARYNGEAL CONSTRICTORS AND SWALLOWING DYSFUNCTION AND PATIENTS QUALITY OF LIFE FOLLOWING RADIOTHERAPY OR CHEMORADIOTHERAPY IN PATIENTS WITH HEAD AND NECK CANCER

DEPARTMENT: Department of Radiotherapy, Dr Ida B Scudder Cancer Centre

NAME OF THE CANDIDATE: Dr. Santanu Samanta

DEGREE& SUBJECT: MD Radiotherapy

NAME OF THE GUIDE: Dr Subhashini John

Objective:

To evaluate the correlation between the radiation dose to the pharyngeal constrictors and swallowing dysfunction using subjective and objective assessment, in patients with head and neck cancer undergoing radiation therapy alone or concurrent chemo radiation therapy.

Methods and materials:

Patients diagnosed to have head and neck cancers and planned for definitive or adjuvant radiation therapy (RT) with IMRT, with or without chemotherapy were screened and 14 patients were included in the study after meeting the inclusion and exclusion criteria. Subjective assessment to assess the Quality of life (QoL) was done

using MD Anderson Dysphagia Inventory (MDADI). Objective assessment of dysphagia was performed with Functional Endoscopic evaluation of Swallowing (FEES). Both assessments were performed before starting RT, midway during the course of treatment and at the end of treatment. The dose volume effects of the pharyngeal constrictors were correlated with FEES assessment and MDADI scores.

Results:

Majority of the patients were male and majority had carcinoma of the buccal mucosa. No patient had complaints of dysphagia or radiological involvement of Pharyngeal constrictors before starting RT. Majority 64% (9/14) had impact on quality of life due to dysphagia at the end of RT, as assessed from MDADI score. 57% (8/14) had severe dysphagia with swallowing liquids and semisolids, as assessed by FEES. Patients with carcinoma of oropharynx, supraglottis and oral cavity received high mean doses and maximum doses to the pharyngeal constrictor muscles. Patients with severe dysphagia assessed by FEES had higher maximum doses to all the pharyngeal constrictors and higher mean dose to superior constrictor compared to those without dysphagia and this was statistically significant. High maximum and mean doses to pharyngeal constrictors were associated with poor quality of life as reflected from MDADI scores.

Conclusion:

Treatment of head and neck cancers with radiotherapy was associated with dysphagia that affects the quality of Quality of life. Severe dysphagia was common with patients

who received high doses to pharyngeal constrictors, most significantly to the superior constrictor. Further studies are essential to assess severity of dysphagia in late setting.

Key Words: Head and neck Cancer, Dysphagia, Pharyngeal constrictors, IMRT, FEES, MDADI, Quality of life.

1. INTRODUCTION

Head and neck cancers are a major cause of morbidity and mortality throughout the world. In India the incidence of head and neck cancers are very high and it is the third most commonly diagnosed malignancy after breast and cervical cancers.(1) Management of early stage head and neck cancers require a single modality where as multi modality approach is essential for advanced stage head and neck cancers.

Radiation therapy which is an important modality in cancer treatment particularly in head and neck cancer has gone through significant evolution. It started with conventional radiotherapy using the Cobalt therapy unit and has evolved to conformal therapy using Linear Accelerator with 3DimensionalConformal Radiation Therapy (3DCRT) and Intensity Modulated Radiation Therapy (IMRT). IMRT has become the standard of care in delivering radiation therapy for head and neck cancers as it helps to minimize dose to normal structures close to the target site, with dose escalation to the tumour at the same time.(2)(3)

Head and neck cancers treated with radiation therapy can cause significant morbidity post treatment in the form of mucositis, xerostomia and dysphagia. Although IMRT can help in reducing dose to the salivary glands and reduce xerostomia and dysphagia, its role in preventing dysphagia by reducing dose to pharyngeal structures and constrictor muscles are controversial.

This study therefore was carried out to evaluate the correlation between radiation dose to the pharyngeal constrictors with subjective and objective assessment of swallowing dysfunction in patients with head and neck cancers undergoing treatment with IMRT.

2. AIMS AND OBJECTIVES

AIMS

To evaluate the correlation between the radiation dose delivered using Intensity Modulated Radiation Therapy (IMRT) technique to the pharyngeal constrictors and swallowing dysfunction using subjective and objective assessment, in patients with head and neck cancer undergoing radiation therapy alone or concurrent chemo radiation therapy.

OBJECTIVES:

Primary : To evaluate the association between the radiation dose delivered using Intensity Modulated Radiation Therapy (IMRT) technique to the pharyngeal constrictors and swallowing dysfunction (early dysphagia and aspiration) in patients with head and neck cancers undergoing radiation therapy alone or concurrent chemo radiation therapy.

Secondary: To assess the Quality of Life (QoL) of patients undergoing radiation therapy, delivered using Intensity Modulated Radiation Therapy (IMRT) technique, either as radical radiotherapy alone or postoperative radiation therapy alone or with chemotherapy, using MD Anderson Dysphagia Inventory (MDADI).

3. **LITERATURE REVIEW**:

Head and neck squamous cell carcinomas are common malignancy with worldwide incidence of more than 550,000 new cases per year in different sub sites of head and neck.(4) It has wide variation considering different anatomic sites and different etiologic factors. Hence head and neck cancers consist of a very heterogeneous group.(5)

The WHO GLOBOCAN Report 2012 also reported a very high 5 year prevalence rate for head and neck cancers in India. Lip &Oral cavity cancers have a 5 year prevalence rate of 12.6%, while for Laryngeal cancers it is 6.8%, Nasopharynx 1.1% and other pharynx 7%. This shows the high burden of head and neck cancers in India with 5 year prevalence rates of nearly 27%.(6)

India does not have a National Cancer Registry that records comprehensive information regarding the cancer incidence or mortality data in India. The National Cancer Registry Programme (NRCP) was started in 1981 by the Indian Council of Medical Research (ICMR). This registry provides information regarding 28 cancer registries located throughout the country. The cancer registries have been classified as population based cancer registries and hospital based cancer registries. Based on the reports of the 7 hospital based cancer registries, head and neck malignancies accounted for around 30% of all cancers in males (table 1) and about 11 % in females. In Chennai the prevalence of Head and neck cancer is about 28% in males and about 11% in females as shown.

Registry		Males			Females	
	All sites	Number of Head and Neck cancers	Proportion of Head and Neck cancers (%)	All sites	Number of Head and Neck cancers	Proportion of Head and Neck cancers (%)
Mumbai	22580	6805	30.1	18528	1673	9.0
Bangalore	11273	3532	31.3	13125	1822	13.9
Chennai	15731	4427	28.1	17499	1832	10.5
Thiruvananthapuram	19219	4798	25.0	18809	1726	9.2
Dibrugarh	2895	1211	41.8	2276	329	14.5
Guwahati	6803	2830	41.6	4679	702	15.0
Chandigarh	2643	598	22.6	2092	100	4.8
Total	**81144**	**24201**	**29.8**	**77008**	**8184**	**10.6**

Table 1 showing prevalence of head and neck cancer in India

The most common head and neck cancers seen in India are tongue and mouth cancers followed by pharyngeal cancers, which is commonly attributable to tobacco chewing practices prevalent in various parts of the country.(7)(1)

3.1. AETIOLOGY OF HEAD AND NECK MALIGNANCY

The most common causes of head and neck malignancies includes consumption of tobacco and tobacco products, alcohol consumption, Human Papilloma Virus infection, dietary factors, exposure to chemicals, precancerous conditions and some other factors like sharp tooth and consumption of spicy food. Amongst all these, consumption of tobacco and tobacco products are the commonest cause. The high prevalence of head and neck malignancies was seen with high consumption of tobacco.(8)Cigarettes, cigars, pipes, bidis and hukkas are the various forms in which tobacco is used for smoking. There are several forms of smokeless tobacco which

have high consumption rates and form a major causative agent for head and neck malignancies. Commonly used forms of smokeless tobacco are tobacco leaves (for chewing), moist snuff, paan or betel quid and gutkha. All these tobacco products have been found to have carcinogens and have been implicated in the causation of a large number of malignancies including head and neck malignancies.(7)(9)

The other important factor in causation of head and neck malignancies is consumption of alcohol. It has been linked to vitamin deficiencies and that also leads to the causation of head and neck malignancies. Consumption of alcohol along with tobacco smoking increases the risk of head and neck malignancies by many folds and has got a synergistic effect. While cigarette smoking and alcohol are the main reasons of head and neck squamous cell cancers in Western countries, it is the smokeless tobacco like khaini, pan, zarda that are common in Asian countries.(10)(11)Head and neck cancers also show field cancerization, where synchronous primary cancers are seen in the entire mucosal tract of the head and neck region. (12) This is common in people who both smoke and drink alcohol, as it causes the entire mucosal tract of the head and neck region to be exposed to carcinogens. (13)

Human Papilloma virus 16 (HPV 16) also plays an important role in head and neck cancers, particularly in oral cavity and oropharyngeal cancers. HPV is a virus that affects squamous epithelial cells. This virus is found in the genitourinary tract and is a major causative factor in the causation of cervical cancers. However, in the past few years, it has also been seen to be associated with a variety of head and neck cancers,

especially the oropharyngeal cancers (tonsils, tonsillar fossa, base of the tongue, and soft palate). (14)The reason for the increase in the incidence of HPV associated oral cancers is the sexual practice of genito-oral sex. Cigarette smoking plays an additive role in the causation of these cancers associated with HPV. (15)

Nasopharyngeal cancers are found to be associated with Epstein Barr viruses (EBV). The incidence of nasopharyngeal cancers is high in areas endemic for the Epstein Barr Virus.(16) EBV titres are nowadays used for determining the tumour burden at the time of diagnosis and have high sensitivity and specificity in diagnosing nasopharyngeal cancers. (17) The EBV DNA titres also play a prognostic role and high titres are associated with a poorer prognosis. (18)Even post treatment EBV DNA titres are associated with high chance of recurrence.(19)

There are many precancerous conditions that play an important role in the causation of head and neck cancers. (20) Leucoplakia and erythroplakia are the two most important premalignant lesions which can transform into invasive carcinoma of the oral cavity.
The other lesions which have also been implicated are submucosal fibrosis, actinic keratosis and lichen planus. Erythroplakia has twenty times more chances for transformation into invasive cancer when compared to leucoplakia.(21) Other factors which have been found to be important in the causation of head and neck cancers are some dietary factors which includes spicy food, sharp teeth and exposure to certain chemicals.(13)

3.2. NATURAL HISTORY OF HEAD AND NECK MALIGNANCY

Most of the cancers of the head and neck region are malignant epithelial tumours. Squamous cell carcinoma is the most common histology seen. These tumours usually begin as surface lesions, but occasionally originate below the surface of the mucosa. The propensity to spread depends on local anatomy and thus varies according to each site. Muscular invasion is common, and tumour may spread along muscle or fascial planes. Tumours may attach to the periosteum but bone or cartilage invasion is a late event as bone and cartilage usually act as a barrier to spread. Tumours that encounter these structures are often diverted and spread along a path of less resistance. (22)

Tumour extension into the parapharyngeal space allows superior or inferior spread from the skull base to the low neck. Perineural invasion (PNI) is observed in squamous cell carcinomas as well as salivary gland tumours, especially adenoid cystic carcinomas. The presence of PNI predicts a poorer rate of local control. Tumours may track along a nerve to the skull base and central nervous system. Patients with PNI may develop neurologic symptoms secondary to nerve invasion or due to entrapment of the nerve. Vascular space invasion is associated with an increased risk for regional and distant metastases.

The risk of lymph nodal metastasis can be predicted by the differentiation of the tumour, size of the primary lesion, presence of vascular space invasion, and density of capillary lymphatic. Recurrent lesions have an increased risk of lymph nodal

involvement. The histology of the tumour also influences the likelihood of lymphatic spread. Low-grade minor salivary gland tumours and sarcomas have a lower risk of lymph node metastases than squamous cell carcinomas.

The relative incidence of clinically positive lymph nodes is determined by the primary site and T stage of the tumour. Well-lateralized lesions spread to ipsilateral neck nodes. Lesions on or near the midline, tongue base and nasopharyngeal lesions, may spread to both sides of the neck, although the risk is higher to the side occupied by the bulk of the lesion. Patients with clinically positive ipsilateral neck nodes are at high risk for contralateral disease, especially if the nodes are large or multiple. The likelihood of retropharyngeal adenopathy is related to the presence of clinically involved lymph nodes and primary site, and is particularly high for nasopharyngeal carcinomas.

The risk of distant metastasis is related mostly to the nodal stage of the disease. The risk is less than 10% for node negative disease and rises to approximately 30% for node positive disease. It is also higher in the presence of nodes below the level of the thyroid notch. The lung is the most common site, accounting for nearly half of the first recognized distant metastases

3.3. HISTOLOGY OF HEAD AND NECK MALIGANANCY

The World Health Organization (WHO) has given a classification for the histological classification of head and neck tumours.(23) Amongst all of these tumours, squamous cell carcinomas and its variants (lymphoepithelioma, spindle cell carcinoma, verrucous carcinoma, and undifferentiated carcinoma) are the most common epithelial malignancies seen in head and neck region. Other tumours which are also commonly seen are salivary gland tumours, lymphomas and sarcomas. However, the incidence of these tumours is very less as compared to squamous cell carcinomas.

3.4. EVALUATION AND DIAGNOSIS

Patients presenting with a likely diagnosis of head and neck malignancy should undergo a thorough history, general medical evaluation, including a thorough head and neck examination. The location and extent of the primary tumour with its dimensions and any clinically positive lymph nodes should be carefully noted. Clinical examination of the primary involves assessing the type of lesion (proliferative, infiltrative and ulcerative), extent and involvement of underlying structures. Examination under anaesthesia (EUA) is also performed for deep lesions that are difficult to assess.

Fine needle aspiration cytology (FNAC) is commonly done for head and neck cancers with neck nodes. FNAC is easy to perform, relatively cheap and with less discomfort

can be done in an outpatient basis. FNAC has a high sensitivity and specificity with a diagnostic accuracy range of 88% to 98%. (24) Non diagnostic aspirations can occur in 5%-15% of the cases where the neck nodes are cystic, commonly found in HPV associated oropharyngeal cancers.(25)Ultrasound guided FNAC or trucut biopsy or excision biopsy of the lymph node is done when repeat FNACs are negative, if there is no obvious primary in the head and neck region or the biopsy from primary is difficult and needs to be done under anaesthesia or requires a tracheostomy.

Evaluation with the help of Naso-pharyngo-laryngoscopy (NPL scopy) is essential for the purpose of assessing the extent of the primary lesion. This is particularly helpful in nasopharyngeal, laryngeal and hypopharyngeal malignancy.

Ultrasonography (USG) evaluation of the neck nodes(26) is essential in evaluation for neck nodes in patients with head and neck cancers as it changes the treatment plan and affects prognosis. Metastatic lymph nodes in head and neck cancers are site specific and depend on the location of the primary tumours most often.USG helps in identification of metastatic nodes with the following features

a. Size: size is one of the most important features to distinguish between reactive and malignant node. Generally malignant nodes tend to be larger than the reactive nodes. In head and neck malignancy nodes above 10mm are considered to be significant according to size criteria.
b. Shape: metastatic nodes tend to be round with ratio of short axis to long axis tends be more than 0.5.Apart from the size, eccentric cortical hypertrophy that

occurs due to focal tumour infiltration with a lymph node is also a diagnostic feature of malignant neck nodes.(27)

c. Metastatic neck nodes tend to have sharp borders
d. They are predominately hypo echoic compared to surrounding structure. Metastatic node from thyroid malignancy may be echogenic due to presence of thymoglobulin. They tend to have calcification unlike benign nodes.
e. Although ancillary feature like matting is common with Tuberculosis, metastatic lymph nodes with diffuse oedema from the primary or pre radiated area may show similar features.

A contrast enhanced computed tomography (CECT) and/or magnetic resonance imaging (MRI) is commonly done to define the extent of locoregional disease. In most cases, CT scan is sufficient and the use of an MRI is reserved only in cases of very early disease. MRI defines the extent of the disease and the soft tissue involvement and help in planning surgery as they give a better delineation of the soft tissues and the extent of the tumour into adjacent structures, fascia, muscles, vessels and nerves. MRI scans are of particular importance in Parotid gland malignancies where the incidence of perineural spread is very high. They can help in visualising the spread of the tumour along the nerves. MRI is also helpful in assessing the skull based marrow invasion, dural invasion, cavernous sinus invasion and retropharyngeal adenopathy. In oral cavity malignancy contrast enhanced MRI helps in accurate extent of tumour within the tongue. Involvement of pre vertebral fascia, characterisation of benign and

malignant salivary gland tumours, recurrence from post treatment changes, features of Paranasal sinuses are other important aspects where MRI is essential.

Contrast CT is essential in gingival, retromolar trigone and buccal cavity lesions as bone erosions are common in this type of malignancy. In the infrahyoid compartment faster speed in CT imaging helps in better visualizations of laryngeal and hypopharyngeal malignancy preventing motion artefacts due to swallowing, that happens in MRI scan.(28) However Diffusion Weighted MRI is often helpful in to detect thyroid cartilage invasion in laryngeal cancers.(29)

The role of a PET scan (Positron Emission Tomography) has been shown to be very useful in the diagnosis of primary tumour as well as recurrences during follow up visits. It has high negative predictive value of 95% to rule out viable disease at the time of follow up. In advanced malignancy it helps to detect the extent of neck nodes and can detect up to 27 % of unknown primaries. The PET scans fused with CT scans gives a better delineation of the anatomical and functional imaging aspects of the tumor and can be used for diagnostic purposes also. They are especially important in detection of metastasis of neck nodes. However, the biggest problem in a PET scan is the non-uniformity of SUV (Standardised Uptake values). Also, the most common tracer used in PET scans is FDG (Flourine deoxy Glucose) which accumulates in areas of high glucose metabolism. Thus, areas of necrosis and hypoxia in the tumours are missed with the use of this tracer as there is no glucose metabolism in these areas.

A chest radiograph should be obtained in all cases to rule out lung metastasis and also to rule out a synchronous primary lung cancer. In case of any suspicion on the chest radiograph, a CT scan of the thorax is indicated for proper characterization of the lung parenchyma. The use of bone scan for evaluation of osseous metastasis is common for nasopharyngeal malignancy. Besides bone scan, USG abdomen is done to assess liver metastasis in cases of locally advanced head and neck cancers. Whole body PET CT scan can also be utilised for evaluate for systemic metastasis.

Before initial treatment, the patient should be evaluated by members of the team who may be involved in the management as well as possible salvage therapy. Head and neck surgeons, radiation oncologists, medical oncologists, diagnostic radiologists, plastic surgeons, pathologists, dentists, speech and swallowing therapists, and social workers may all play a role. The treatment options are discussed and recommendations are presented to the patient who makes the final decision.

3.5. STAGING OF HEAD AND NECK CANCERS

The different sub sites of head and neck cancers are staged differently based on TNM classification. This classification was first devised by Pierre Denoix between 1943 and 1952. This was further developed and maintained by the Union for International Cancer Control to achieve global consensus regarding staging of cancers. (30) Currently the 7th edition has been published in 2009 and adopted for practice from 2010 onwards.(31) The staging mentioned below is taken from AJCC- TNM classification(32) of malignant tumours published in seventh edition 2009.

The cancer of the head and neck are staged as follow

Staging of Lip and Oral cavity

T – Primary Tumour

Tx Primary tumour cannot be assessed
T0 No evidence of primary tumour
Tis Carcinoma in situ
T1- tumour that is 2 cm or less in greatest dimension
T2- tumour that is more than 2cm but less than 4cm in greatest dimension
T3-tumour more than 4cm in greatest dimension
T4a(lip) tumor invades through cortical bone, inferior alveolar nerve, floor of the mouth or skin of the chin or nose.
T4b (oral cavity) tumour invades the cortical bone, involving deep/extrinsic muscle of tongue, maxillary sinus or skin of the chin or nose
T4b (lip and oral cavity) tumour invades masticator space, pterygoid plates, or skull base of involves internal carotid artery

N- Regional Lymph nodes

Nx Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in a single ipsilateral lymph node,3cm or less in greatest dimension
N2 Metastasis as described below:
N2a Metastasis in a single ipsilateral lymphnode, more than 3 cm but not more than6 cm in greatest dimension
N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3 Metastasis in a lymph node more than 6 cm in greatest dimension

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

Staging of the Pharynx

Staging of Nasopharynx

T1 Tumour confined to the Nasopharynx, or tumour extends to oropharynx and/or nasal cavity without parapharyngeal extension
T2 Tumour with parapharyngeal extension
T3 Tumour involves bony structures of skull base and or Paranasal sinuses
T4 Tumour with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, or with extension to the infratemporal fossa/masticator space

Staging of Oropharynx

T1 Tumour 2 cm or less in the greatest dimension
T2 Tumour more than 2 cm but not more than 4 cm in the greatest dimension
T3 Tumour more than 4 cm in greatest dimension or extending to lingual surface of the epiglottis
T4a Moderately advanced local disease with invasion of larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible
T4b Very advanced local disease with invasion of lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or base of the skull or encasing the carotid artery

Staging of the Hypopharynx

T1 Tumour limited to one subsite of hypopharynx and or 2 cm or less in the greatest dimension
T2 Tumour invades more than one subsite of the hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest dimension without fixation of hemilarynx
T3 Tumour more than 4 cm in greatest dimension or with fixation of hemi larynx or extension to esophagus
T4a Moderately advanced local disease with tumor invading thyroid or the cricoids cartilage, hyoid bone, thyroid gland, or central compartment soft tissue
T4b Very advanced local disease that invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

N- Regional nodes for Nasopharynx
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Unilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa, and/or unilateral or bilateral, retropharyngeal lymph nodes, 6 cm or less, in greatest dimension
N2 Bilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa
N3 Metastasis in a lymph node(s) >6 cm and/or to supraclavicular fossa
N3a Greater than 6 cm in dimension
N3b Extension to the supraclavicular fossa

Regional Nodes for Oropharynx and Hypopharynx
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in the greatest dimension
N2 Metastasis in single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N2a Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension
N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3 Metastasis in a lymph node more than 6 cm in greatest dimension

Primary Tumour (T) Supraglottis
TX Primary Tumour cannot be assessed
T0 No evidence of primary Tumour
Tis Carcinoma in situ
T1 Tumour limited to one subsite of supraglottis with normal vocal cord mobility
T2 Tumour invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, valleculae and medial wall of pyriform sinus) without fixation of the larynx
T3 Tumor limited to larynx with vocal cord fixation and/or invades any of the following: post cricoid area, pre epiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage
T4a Moderately advanced local disease that invades through the thyroid cartilage and/ or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
T4b Very advanced local disease invading prevertebral space, encases carotid artery, or invades mediastinal structures

Glottis
T1 Tumour limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
T1a Tumour limited to one vocal cord
T1b Tumour involves both vocal cords
T2 Tumour extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility
T3 Tumour limited to the larynx with vocal cord fixation and/or invasion of paraglottic space, and/or inner cortex of the thyroid cartilage
T4a Moderately advanced local disease invading through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
T4b Very advanced local disease invading prevertebral space, encases carotid artery, or invades mediastinal structures

Subglottis

T1 Tumour limited to the subglottis

T2 Tumour extends to vocal cord(s) with normal or impaired mobility

T3 Tumour limited to larynx with vocal cord fixation

T4a Moderately advanced local disease invading the cricoid or thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)

T4b Very advanced local disease invading the prevertebral space, encases carotid artery, or invades mediastinal structures

Regional Lymph Nodes (N)

NX Regional lymph nodes cannot be assessed N0; no regional lymph node metastasis

N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension

N2 Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension

N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension

N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension

N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension

N3 Metastasis in a lymph node, more than 6 cm in greatest dimension

3.6. OVERVIEW OF THE MANAGEMENT OF HEAD AND NECK CANCER

The management of head and neck cancer depends on the site, stage of the disease along with general condition of the patient. The different sub sites in head and neck cancers have a different prognosis depending on stage, histology and anatomical location of the tumour. It is mostly the T stage of the disease and the presence or absence of nodal metastasis which serve as important prognostic factors related to survival. Other factors which have been seen to be important prognostic indicators are the histology of the tumour and occasionally the sex predilection of tumour.

Advanced T stage is associated with worse local control and overall survival. Also advanced N stage predicts increased risk of distant metastasis and worse survival. Presence of distant metastasis (M1) at the time of presentation indicates poor prognosis. The presences of bone erosion, cranial nerve palsy or lower nodal level are all poor prognostic factors. Histology wise, non keratinizing and undifferentiated carcinomas are more radiosensitive and have a better prognosis than keratinizing squamous cell carcinoma

Early stage head and neck cancers are managed with single modality like surgery or radiotherapy but locally advanced requires a combination of modalities of therapy. The selection of the modality depends on the site, stage, operability and general performance of the patient. Surgery is the mainstay of the treatment for early stage head and neck cancers and radiation therapy is required only if risk factors are present.(33) Sometimes radiation therapy alone is used for management of early stage cancer as surgery increases the morbidity and quality of life and also if the patient is

unwilling or medically unfit for surgery. In locally advanced head and neck cancers the management involves a multimodality approach with definitive chemo radiotherapy or surgery followed by radiotherapy with or without chemotherapy based on HPE. Trials have consistently demonstrated that combined treatment of radiation therapy with concurrent Cisplatin whenever indicated is superior compared to only radiation therapy in terms of local tumour control and overall survival.(36).In very advanced stage disease; palliative radiation therapy is also used to control the symptoms.

3.6.1. SURGERY

Surgery is one of the modalities of treatment in treatment of head and neck cancers. The primary goal of surgery is to remove the tumour with adequate margins at the same time retain the functionality of individual organs. Minimally invasive surgery may be used for early stage disease. Locally advanced carcinoma requires adjuvant treatment after surgery. Unresectable tumours can be defined as those tumours that cannot be removed without unacceptable toxicities, as mentioned in NCCN guidelines. Tumours that involve the cervical vertebra, skin, brachial plexus, deep muscles of the neck or carotid artery are considered inoperable as complete removal of the tumour is not possible on anatomic grounds.

Along with the primary tumour resection, neck dissection is also performed. Historically neck dissection was classified as radical or modified radical procedure.

Presently the procedure is classified as selective neck dissection or comprehensive neck dissection. The final HPE of primary tumour and neck dissection determines the adjuvant treatment (chemo radiation therapy or radiation therapy).(37)

In general compared to radiation therapy, surgery involves limited amount of tissue exposed to treatment, shorter treatment time and less late treatment complications. Achieving an adequate margin during surgical resection is of utmost importance. Adequate margin is defined as clear resection margin with at least 5mm or more from the invasive tumour. Close margins is defined as one less than 5mm.

3.6.2. POST OPERATIVE RT WITH OR WITHOUT CHEMOTHERAPY

The role of adjuvant therapy in post operative patients depends on risks factors as shown in clinical trials RTOG 9501 and EORTC22931. (38)(39) Both the trials showed that patients with extra capsular nodal spread and or positive margins had improved overall survival with chemoradiation therapy compared to radiation therapy alone. Patients with multiple regional nodes but without any extra capsular spread did not show any survival benefit with addition of chemotherapy to radiation therapy. Indications of only post operative radiation therapy are multiple positive nodes, pT3 or T4 primary disease and positive level 4 and 5 nodes in oral cavity and oropharyngeal carcinomas. Commonly used chemotherapy is Cisplatin. Carboplatin or biological therapy can also used in case of poor performance status of the patients.

3.6.3. CHEMORADIATION

The rational for combining chemotherapy with radiation therapy in treatment for head and neck cancer is to sensitize the tumour to radiation therapy by inhibiting tumour repopulation, killing hypoxic cells and sterilizing micro metastatic disease outside the radiation field. Fractionated radiation therapies also in return sensitize tumours to chemotherapy by inhibiting the repair of drug induced damage.

With this concept in mind there were early trials that showed the benefits of chemo radiation therapy. Aldestein et al (40)showed that patients with unresectable head and neck cancers when with treated with concurrent chemo radiation therapy reported to have increased median survival compared to those with only radiation therapy alone.

RTOG 91-11 trial also showed that larynx preservation rate and locoregional control was significantly improved with concurrent chemo radiation therapy compared to induction chemotherapy or radiation therapy alone.(39)

Hence in a patient with locally advanced head and neck cancer, combined modality with radiation therapy and chemotherapy is the standard of care.

3.6.4. CHEMOTHERAPY

Chemotherapy in head and neck cancer can be used as neoadjuvant therapy, concurrent with radiation therapy or as palliative therapy.

The history of use of chemotherapy started long ago, with single agent chemotherapy or combination chemotherapy along with radiation therapy. Chemotherapeutic agents like Mitomycin, 5 Fluouracil had severe toxicities when used with radiation therapy. (40) Of all the agents, Cisplatin became the drug of choice for use concurrently with radiation therapy. Trials with concurrent chemotherapy Cisplatin showed significant benefit in head and neck cancers. The MACH-NC meta-analysis showed the benefit of adding concurrent chemotherapy to radiation therapy in head and neck cancers and results showed an improvement in overall survival rates at 5 years with the addition of concurrent chemotherapy.(41)

There is also a role of neoadjuvant chemotherapy in locally advanced head and neck cancers. Neoadjuvant chemotherapy downsizes the tumour that further helps in surgery or radiation therapy. The TAX 323 and 324 trials (42) show that in locally advanced unresectable head and cancers, neo adjuvant chemotherapy with Docetaxel, Cisplatin and 5-Fluorouracil, had long term survival benefit in patients with unresectable disease.(43)(44)

Chemotherapy with adjuvant radiation therapy after surgery is used for patients with high risk factors as mentioned above. (45)(46)

In metastatic head and neck cancers chemotherapy is used as palliative agent. Drugs like Docetaxel, Paclitaxel, Gemcitabine, Methotrexate are used in palliative or recurrent head and neck cancers.(47)(48)

3.6.5. BIOLOGICAL THERAPY

Squamous cell carcinomas of the head and neck often over express epidermal growth factor receptor (EGFR).This high expression of EGFR is associated with poor prognosis. Cetuximab is a biological targeted therapy that binds to EGFR receptor. Boner et al showed that treatment of loco regionally advanced head and neck cancer with high dose radiotherapy and Cetuximab improves locoregional control and reduces mortality without increasing common toxic side effects.(49) Cetuximab is used for patients who cannot tolerate concurrent chemotherapy in view of poor performance status.

Nimotuzumab is another biological agent targeting EGFR receptor that is demonstrated to be safe and effective when combined with chemotherapy or chemoradiation therapy in head and neck cancers(50). In metastatic head and neck cancers Tyrosine Kinase Inhibitors like Gefitinib is also used.(47)

3.6.6. RADIATION THERAPY

Radiation therapy is an important and potential curative modality in head and neck cancers. For locoregional disease RT is often used in combination with chemotherapy as definite organ preservation approach or after surgery as adjuvant therapy.

CONVENTIONAL RADIATION THERAPY

Radiation therapy has evolved from the conventional era of two dimensional conventional planning to the present day era of 3 dimensional conformal planning. Initially, patients were planned with 2 dimensional conventional methods of planning in which an X ray was taken to define the field borders. The field borders were placed depending on the anatomical extent of the tumour and the nodal spread of the disease. In the conventional planning methods, it is difficult to reduce the dose to the adjacent normal structures, without compromising the dose to the primary tumour. The radiation therapy beams deliver the same dose throughout to the primary tumour and to the adjacent normal structures. Customised blocks may be used to decrease the radiation dose to the normal tissue. However, the process of making customised blocks is very cumbersome and even with their use; the normal tissue still receives a very high dose. Thus, the therapeutic index for such a planning technique is very small with very high rates of complications due to increased radiation dose to normal tissue.

CONFORMAL RADIATION THERAPY

The concept modulating the fluence of the radiation beam to achieve a desired dose distribution was first given by Brahme et al in 1982. (51)(52)However, it was not till the early 21st century that fluence modulation was used in delivering radiation therapy beams. It was with the start of CT planning in radiation therapy which led to the development of Intensity Modulated Radiation Therapy (IMRT). Since the development of this modality of delivering radiation therapy, the most important

aspect which has improved is the Therapeutic ratio. With the modulation of the dose fluence, it is now possible to give higher dose to the tumour and lesser dose to the normal tissue which is located in close proximity to the tumour.

In head and neck malignancies, several critical organs at risk are found to be in very close proximity to the target volume. Also there is a lot of in homogeneity in the head and neck region which can affect the dose and delivery of radiation. Often depending on the site and extent of primary disease the tumour surrounds the normal tissues or lies in close proximity to critical structures and makes it difficult or impossible by conventional radiation therapy to deliver high doses to the tumour tissue without giving unacceptable doses to the adjacent normal structures. However, with IMRT, it is practically possible to decrease the normal tissue dose while delivering high dose to the tumour. One of the main advantages of IMRT in head and neck cancers is sparing of parotid gland and prevention of late xerostomia, at the same time escalate dose to the tumour.(53) Intensity Modulated Radiation Therapy (IMRT), thus, is presently considered the standard of care in managing head and neck malignancies. IMRT can be delivered using different methods like sequential two phases or single phase Simultaneous Integrated Boost (SIB) technique.

All these techniques of delivering IMRT have the same treatment volumes comprising of the high risk volume (consisting of the area of tumour and area for high risk of disease spread) and a low risk volume (area which will be irradiated prophylactically to prevent the spread of the disease). In few instances like nasopharyngeal carcinoma,

there is also an intermediate risk area identified which is treated to doses in between the high risk and low risk area.

3.7. SIDE EFFECTS OF RADIOTHERAPY

Improvement in the loco-regional control was largely due to intensification of the treatment with radiation therapy dose intensification and addition of chemotherapy. The improvement in overall survival was noted with several trials that studied concurrent chemo radiation therapy for head and neck malignancy. With increased in survival, the heath related to quality of life has become very important to these patients. Patients expect a good quality of life without any compromise in treatment outcomes following the treatment of head and neck cancers. There are many side effects that happen during as well as after the course of radiation therapy. Common side effects following the radiation therapy to head and neck cancer patients occur as early and late side effects. The chances of these complications and its severity depend on a number of factors including total dose of radiation delivered, time and the region where radiation therapy was received(54). These side effects can be described as follows:

a. Xerostomia
b. Mucositis
c. Candidiasis
d. Dysguesia
e. Dental caries
f. Osteroradionecrosis

g. Trismus
h. Oral Pain
i. Dermatitis, soft tissue fibrosis
j. Dysphagia

Out of all these problems, xerostomia and dysphagia are common problems that happen in patients undergoing radiation therapy both as acute and late effect of radiation therapy.

a. Xerostomia: It is also known as dryness of the mouth due to decreased saliva secretion and is one of the most common of all the side effects for patients receiving radiation therapy. (55) Xerostomia occurs as major and minor salivary glands in our body are damaged due to radiation therapy for the cancer treatment. The problems associated with xerostomia include difficulty to speak, difficulty in eating and increased risk of dental caries. Saliva helps to protect the teeth and absence of saliva in there is increased in chances of dental caries formation. The use of IMRT technology in radiation therapy has greatly reduced xerostomia(56). The PARSPORT trial which is a Phase III randomised trial showed that radiation therapy with IMRT reduces patient reported xerostomia, allows recovery of salivary flow and improves the quality of life after treatment in head and neck cancers, compared to conventional radiation therapy. Xerostomia can be treated by mechanical or taste stimulants, saliva substitutes and systemic therapy. Alternative methods like acupuncture have also been used to reduce xerostomia. While systemic therapy such as use of Pilocarpine increase the salivary flow, saliva substitutes improve the

xerostomia without any effect of salivary hypo function. The use of Pilocarpine has been most useful when used during radiation therapy(57).

b. Dysphagia: It is defined as difficulty to swallow solids or liquids. This can happen if the primary disease in head and neck cancers causes impairment in functioning of the swallowing structures as well or as a complication due to treatment. Dysphagia is often an underestimated problem in head and neck cancer patients.(58) Surgery for locally advanced cancer can cause swallowing problems by limiting the actions of various muscles associated with swallowing. Further radiation therapy after surgery produce radiation induced fibrosis, dysphagia and xerostomia that increase the difficulty in swallowing capacity. In patients with radical chemoradiation therapy the incidence of dysphagia is approximately 50 % and this is greatly reduced when treated with IMRT compared to conventional radiation therapy.(59)(52) Several attempts have been made to reduce radiation therapy doses to swallowing muscles to minimise the functional problem of dysphagia.

Dysphagia is a common complication associated with radiation therapy in the head and neck cancers. With clinical trials trying to improve local control with different fractionation schedules and concurrent chemo radiation therapy, the toxicity of mucositis followed by dysphagia became increasing common.(55) Although increase toxicities following these intensified treatments could be recorded in CTC criteria, objective measures for assessment of complications were not done routinely during

earlier times. A number of clinician administered questionnaire was started to review the complications and functional impairments following concurrent chemo radiation therapy(60). Objective measurements of voice, speech and swallowing functions were also conducted with the help of video fluoroscopic assessment(61)(62).

3.8. DYSPHAGIA

Dysphagia can be described as swallowing disorder resulting from neurological or physiological impairment of the oral, pharyngeal or esophageal mechanisms.(63)

Normal swallow has four coordinated steps as follows:

a. Oral preparatory phase
b. Oral transit phase
c. Pharyngeal phase
d. Esophageal phase

The first three of these are known as oropharyngeal phase.

During the oral preparatory phase food is crushed and mixed with saliva to form a bolus which is positioned on the tongue for transport. For solids, the food is positioned with the help of the tongue and mixed with saliva. The pharynx and larynx are at rest during this time. The airway is open and normal free breathing continues

During the second phase, the bolus prepared gets ready for the transit. The tongue creates an anterior and posterior propulsion movement that helps the bolus to move

towards the pharynx. During this movement the sensory receptors of the oropharynx and the tongue get stimulated and swallowing reflex gets initiated. As the food viscosity thickens greater muscle activity is required to squeeze the food back. Oral transit phase typically lasts for 1-1.5 second and increases with the increased viscosity of the food.

Swallow reflex: As soon as food reaches the anterior faucial pillars at level of valleculae, the pharyngeal swallow gets stimulated with the help of sensory receptors that reaches the medulla and the pharyngeal motor pattern is initiated. For the younger individuals the faucial pillars are the most sensitive area where as for older individuals the middle of the base of the tongue is the most sensitive area.

During the third phase, a number of simultaneous and coordinated activities take place that helps in swallowing. First the soft palate stretches back to close the velopharyngeal port and prevent the reflux of food contents into the nasal cavity. This is followed by elevation and anterior movement of the hyoid bone and the larynx. The anterior movement of the larynx helps in opening of the esophagus and elevation of the hyoid protects the airway. Closure of the various laryngeal structures begins in the below upwards. Epiglottis inverts and come in contact to prevent the airway, the pharyngeal muscles contracts. Once the food is directed around the epiglottis, there is relaxation the esophageal sphincter, the pharyngeal phase ends and breathing is initiated.

3.8.1. **SWALLOWING ABORMALITY SECONDARY TO RADIATION THERAPY**:

The most important complication in patients having dysphagia after chemoradiaton therapy is aspiration. (64) Nguyen et al has reported that prevalence of sever aspiration in patients having dysphagia is almost 33%. Eisbruch et al also reported that post chemo radiation therapy, one of the most common reasons for morbidity is aspiration pneumonia.(65)

Dysphagia can occur due to abnormalities in oral preparatory and pharyngeal phase:

Dysphagia in the oral preparatory phases can be due to the following

- Limitations due to closure of lip
- Loss of cheek muscles after surgery
- Trismus
- Weakness of tongue movements due to disease
- Decreased sensation
- Delay in initiating the food preparation
- Decreased saliva post radiation therapy

Dysphagia in pharyngeal phases can occur due to

- Edema in the epiglottis, slower movement and inversion
- Decreased laryngeal movement and elevation
- Decreased opening of cricopharyngeus muscle and increased pharyngeal residue

One important reason for dysphagia, but less mentioned in literature is the formation of stricture in the hypopharyngeal region. The risk factors for this hypopharyngeal stricture include female sex, twice daily radiation and hypopharyngeal malignancy. The efficacy of dilatations has limited benefits.(66)

3.8.2. RISK FACTORS FOR POST RADIATION SWALLOWING ABNORMALITIES

There are several risk factor identified to cause dysphagia in patients with head and neck radiation therapy. Structures within the radiation port as well as the technique of radiation therapy influence the chances of dysphagia.

In 2002, Eisbruch et al,(65) aimed to assess the swallowing functions objectively, in locally advanced head and neck cancers. The study concluded that after chemo radiation therapy there was significant swallowing dysfunction that was associated with aspiration in these groups of patients. Video fluoroscopy was the validated method for assessing the swallowing function allowing viewing and recording of the structures and dynamics of the swallowing process. Examinations were performed and interpreted by a radiologist and a speech-language pathologist. Each subject was asked to swallow multiple trials of various food consistencies in varying amounts during the swallowing assessment. The examinations were recorded, and analysis of the three phases of swallowing - oral, pharyngeal, and esophageal- was subsequently assessed with focus on food bolus manipulation, passage, motility and timing(67).

Thus the objective and subjective methods to assess early and late toxicities in patients with locally advance head and neck cancers undergoing radiation therapy came into practice. With these assessment tools, early and late pharyngeal toxicities became a limiting factor for intensification of treatment with dose escalation in conventional radiotherapy and chemotherapy.

Radiation therapy with IMRT technique became one of the major tools to reduce the toxicities. With IMRT, it was possible to produce highly conformal dose distribution, and reduce dose to the oral mucosa, thereby limiting the chances of dysphagia. Several studies showed that IMRT significantly reduced the rate of dysphagia(68).
Study by Feng et al showed that there was dose-volume- effect relationship with IMRT treatment and reducing the doses to the pharyngeal constrictors can reduce dysphagia and aspiration.(69)

Levendag et al (70)also showed that there exist a dose effect relationship between dose to the pharyngeal constrictor muscles and dysphagia. Dysphagia can be minimised by reducing dose to the pharyngeal constrictor muscles.

Eisbruch et al in 2004(65)(71) showed that swallowing assessment showing video fluoroscopic abnormalities were attributable to the dysfunction of the circular pharyngeal constrictors, longitudinal pharyngeal muscles, suprahyoid muscles that pull the hyoid-laryngeal complex superiorly and the muscles that pull the base of the tongue backward. Out of all these, the circular pharyngeal constrictors and larynx were the major cause that limits the swallowing function. Post radiation therapy assessment with MRI showed that there was significant thickening noted, representing

oedema and fibrosis to the pharyngeal constrictor muscles. This was confirmed by further studies that assessed radiological changes post radiation therapy in head and neck cancers(72).

The epiglottis, aryepiglotic folds, arytenoids, true and false vocal cords also coordinate in swallowing function to prevent aspiration(73). The laryngeal closure reflex mediated through the superior laryngeal nerve is an important protective mechanism against aspiration and this is absent in many patients with head and neck cancers(67). The sensation of food particles entering larynx provides a vital mechanism to prevent aspiration by evoking a cough and adductor response. This mechanism is affected in many patients undergoing radiation therapy and thus has a higher chance of aspiration followed by pneumonia.

Apart from the pharyngeal constrictors and larynx, no radiologic changes in MRI were noted in other structures that can cause video fluoroscopic changes for swallowing dysfunction. The circular pharyngeal constrictors and the laryngeal adductors which lie close to the mucosa and submucosa are primarily affected after radiation therapy. There is also loss of elasticity of the muscle after radiation therapy, with accumulation of pro-inflammatory cytokines that can explain the video fluoroscopic abnormalities.(65)

After the dysphagia and aspiration related structures were identified, several studies assessed the correlation between the dose delivered to these organs and the severity of dysphagia.(74) Study by Anderson et al(75) aimed to validate the Quantec recommendations for dose to larynx during IMRT to prevent acute dysphagia. This

study showed that restricting the doses to constrictor reduces the chances of dysphagia in patients undergoing radiation therapy. Study by Bhide et al aimed to see the correlation between dose to the pharyngeal constrictors and impact of late dysphagia on Quality of life. (76) This study however didn't show any significant correlation between the dose to pharyngeal constrictors and patient reported or observer assessed dysphagia.

3.8.3. COMPLICATIONS OF DYSPHAGIA

The most important complication of dysphagia is aspiration that leads to pneumonia. Dysphagia can also lead to chronic bronchial irritation that leads to chronic cough. Pneumonia following aspiration can be serious and can lead to deaths in patient having severe dysphagia.(77)

Late and chronic dysphagia leads to the use of tube feedings that may limit the nutritional demand of patients. Chronic and late dysphagia leads to poor quality of life and worsening of overall well being of the patient.

3.8.4. PREVENTION, TREATMENT AND REHABILATATION

Prevention to dysphagia involves treatment with IMRT that can spare the swallowing structures or reduce the dose to pharyngeal constrictors. Early detection of dysphagia can help to prevent serious side effects of aspiration by alternative feeding procedure and neck rehabilitation exercises. There are several ways like postural techniques, motor exercises, swallowing manoeuvres and changes in diet that can help patients improving dysphagia.(77)

3.9. ASSESSMENT OF DYSPHAGIA

Patients with head and neck cancer often experience complaints of dysphagia. Patients can also develop this complaint at the end of treatment due to the side effects of the treatment. The severity of dysphagia depends on various factors like size and location of cancer, nature of surgery and reconstruction and radiation therapy. The symptoms that patient experience may be (78)

a. Multiple swallows to clear the food
b. Throat clearing while eating
c. Pain and dryness whole eating
d. Coughing or choking

There are various ways for assessment of dysphagia.(77) The subjective method is a way of assessment of impact of dysphagia on quality of life (QOL). There are various

ways of subjective assessment with the help of questionnaires that are developed and validated to address the problem of dysphagia. The objective assessment of dysphagia can be done by Video fluoroscopy study of swallowing (VFSS), modified barium swallow study (MBSS),functional endoscopic evaluation of swallowing (FEES).(67)(77)

SUBJECTIVE ASSESSMENT

The subjective assessment is based on the rationale that along the tumour control rate, overall survival rate, there are several problems that impact the quality of life in patients with head and neck cancers. One of the most popular tool to assess quality of life in head and neck cancer is the FACT-H&N score that reports quality of life in patients with laryngeal cancer.(79) Quality of life was also assessed by developing QOL-RTI that was valid and reliable tool for the assessment of patients with head and neck cancer undergoing radiation therapy. (80)

The European Organisation for research and treatment of cancer quality of life Questionnaire (EORTC QOL) H&N35 developed a questionnaire to assess the quality of life in head and neck cancer patients.(81) This questionnaire was used and validated in many trials(82)(83) and the recent update started that with the advent of multimodality treatment, several new modifications need to be considered for the EORTC QOL H&N35.(84) The results from the questionnaire in EORTC QOL H&N 35 showed that compared to conventional radiation therapy, treatment with IMRT had

significant better outcome in sense of global QoL, physical well being, swallowing, speech, dry mouth, feeling ill etc.

However, this questionnaire lacked dysphagia specific assessment. Hence to assess impact of dysphagia on quality of life, MD Anderson Dysphagia Inventory (MDADI) was developed. (85)It was adopted and validated in several studies to assess the quality of life in patients with dysphagia in head and neck cancers.(86)(87)

The MDADI had 20 questions that assessed the global functioning, functional, emotional and physical aspect of daily activities in patients with dysphagia. Each question had 5 choices and an overall higher MDADI score represented better day to day functioning and better quality of life (QoL) in patients with head and neck cancers. The questionnaire also had 3 specific questions that assessed the severity of dysphagia. (85)

This MDADI was also adopted by Bhide et al, that assessed the correlation between dose to the pharyngeal constrictors and quality of life with dysphagia following chemoradiation therapy in head and neck cancers.(76) The study showed that patients undergoing chemoradiation therapy for head and neck cancers had dysphagia evident from the questionnaire and there was significant correlation between the objective assessment and MDADI. (74)(88)Several other studies also adopted the MDADI for assessment of QoL in patient with Dysphagia, undergoing treatment with chemo radiation therapy.(70)(89)(90)

OBJECTIVE ASSESSMENT

The objective assessment of dysphagia is commonly performed by video fluoroscopy swallowing study (VFSS) or Functional Endoscopic Evaluation of Swallowing (FEES).(91)

The Video fluoroscopy examination of swallowing provides real time visualization of the oral cavity, oropharynx, laryngo-pharynx, and esophagus while using various consistencies and volume of barium coated materials. These coated food materials are ingested and their movements through the oral and pharyngeal cavities are viewed on monitor in the radiology suite. VFSS is an excellent tool for assessment of swallowing functions and defining functional deficits and degree of aspiration.

However VFSS has several disadvantages. First of all, the procedure is done in Radiology suite that required fluoroscope, monitor and skilled personnel all of which can be very expensive. There are also risk of radiation exposure to staff and appropriate positioning and adequate cognitive functioning are essential for VFSS assessment. With these limitations FEES became more popular and it was well tolerated, easy to perform with less complications like discomfort, gagging , vomiting.(92)

Several studies have showed that assessment of swallowing by FESS was well accepted tool for assessment of dysphagia.(93)Kelly et al showed that severity of penetration aspiration scale in patients can be better evaluated with FEES than VFSS. (94)The study by Rao et al aimed to determine the sensitivity and specificity value for

different parameters like pharyngeal residue and laryngeal penetration also confirmed that FEES is comparable to VFSS for assessment of dysphagia. Hence FEES is considered a standard tool for assessment of swallowing and aspirations. (95)

The FEES assessment established by Langmore et al is quite a comprehensive evaluation of swallowing function and has mainly three components

a. Structural movements, sensory status and anatomic support of swallowing
b. Ability to swallow solid food and liquid
c. Response to different alterations of the path , the way bolus is swallowed

The assessment of FEES is done in outpatient clinic and reported as described in the policy statement by the Royal College of Speech and Language Therapists. It provides direct visualization of different anatomical structures like Nasopharynx, base of the tongue, vocal cords and larynx. The important functions like management of secretions, muscular functions of pharyngeal constrictors can be assessed along with identifications of pooling, laryngeal penetration, spillage, aspiration and laryngo-pharyngeal reflux.(96)

4. METHODS AND MATERIALS

This is a prospective observational study conducted in Department of Radiotherapy, Christian Medical College (CMC). Patients diagnosed to have head and neck cancers without any complaints of dysphagia and planned for treatment with IMRT were included into the study according to the following criteria.

Inclusion Criteria:

1. Patients with age more than 18 years
2. Patients diagnosed to have biopsy proven malignancy of head and neck cancers
3. Planned for radical radiotherapy with or without chemotherapy
4. Planned for post operative radiotherapy with or without chemotherapy
5. Radiation therapy with intensity modulated radiation therapy (IMRT)
6. Willing for evaluation of their swallowing function with FEES
7. No baseline swallowing dysfunction
8. No evidence of disease in the pharyngeal constrictors

Exclusion Criteria:

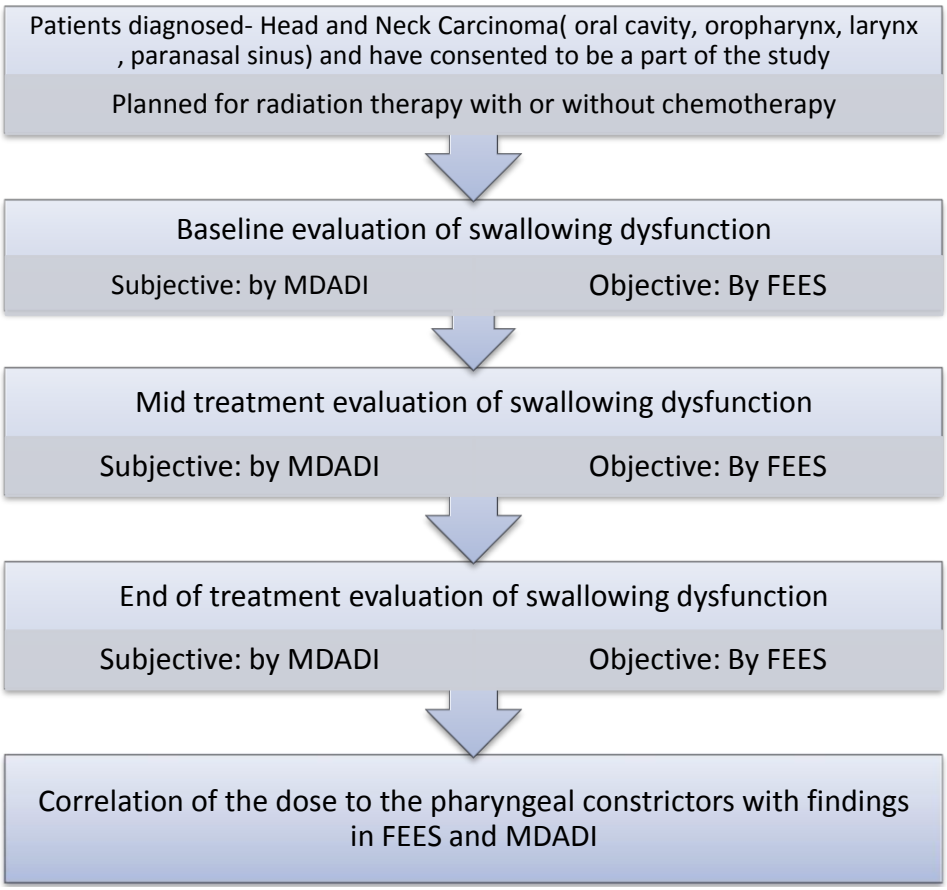
1. Patient with prior radiotherapy
2. Patient planned with conventional radiotherapy
3. Patient with carcinoma Nasopharynx or Hypo pharynx
4. Patient with histology of lymphoma, sarcoma.

The proposed study was presented in the Institutional Review Board (IRB) which includes Research committee and Ethics Committee and approval was obtained (copy enclosed).

4.1. STUDY DESIGN:

This study assessed the quality of life in patients diagnosed to have head and neck cancers undergoing radiation therapy with IMRT. Patients were subjectively assessed for dysphagia with MDADI and objectively with FEES before starting of radiation therapy, midway and end of radiation therapy. The radiation dose to the pharyngeal constrictors was correlated with the swallowing dysfunction in FEES and the MDADI.

Study work flow:



4.2. SAMPLE SIZE:

Patients diagnosed with head and neck cancers and planned for radiation therapy with IMRT were screened. Among the 22 patients screened, 14 patients who met the inclusion and exclusion criteria were selected for the study. These 14 patients underwent treatment with radiation therapy with or without chemotherapy from March 2015 to August 2015 by IMRT technique either as radical treatment or as postoperative therapy. Seven patients were not included as they had evidence of involvement of the pharyngeal constrictors in the planning CT scan and one patient was not included as she had history of prior radiation.

4.3. RADIATION THERAPY:

Patient received radiation therapy either as definitive intent or post operative setting. They were explained regarding the process of radiation therapy with IMRT technique, costs and benefits, related side effects and time duration of therapy. They were explained the side effects of chemotherapy with Cisplatin if indicated, after clearance from Cardiology for the same. Audiogram was performed to assess any underlying hearing loss, before chemotherapy. Metastatic work up and dental clearance was obtained for all patients. In post operative setting, radiation therapy was initiated only after healing of the surgical scar with an average period of 2- 3 weeks.

Radiation therapy planning

Immobilization: Patients were positioned supine on the simulator couch and Orfit Raycast was used for immobilization. The 3 points were marked on the Raycast on the simulator using the anterior and lateral lasers. Planning CT was carried out with the same set up. CT scan was obtained 3mm slice thickness from vertex to T4 vertebral level, with IV contrast. The planning CT was imported to the Eclipse Contouring stations for segmentation. Images were registered and segmentation of the targets volumes and organ at risks were done using standard guidelines.(97)

Contouring of the constrictor muscle: Fig 4.1

Contouring or segmentation of the pharyngeal constrictors were done on the planning CT according to the guidelines as described by Eisbruch et al. (69) and Bhide et al.(76) Three parts of the pharyngeal constrictors were identified. Each of the pharyngeal

constrictors was outlined as an arch shaped structure with concavity facing anteriorly, in line with the mucosa. Posterior border of each of the muscles was prevertebral muscle. This was done using 3mm brush in the Eclipse contouring tool.

Superior constrictor (SC) was outlined from the caudal tips of the pterygoid plates and the caudal extent was superior end of the hyoid. Middle constrictor (MC) was outlined from superior end of the hyoid bone to inferior end of the hyoid bone. Inferior constrictor (IC) was outlined from inferior aspect of the hyoid to inferior end of the cricoid cartilage. The three pharyngeal constrictor structures were combined to create total constrictor unit (TC). The segmentation of the pharyngeal constrictors can be seen as below:

Segmentation of Pharyngeal constrictor muscles

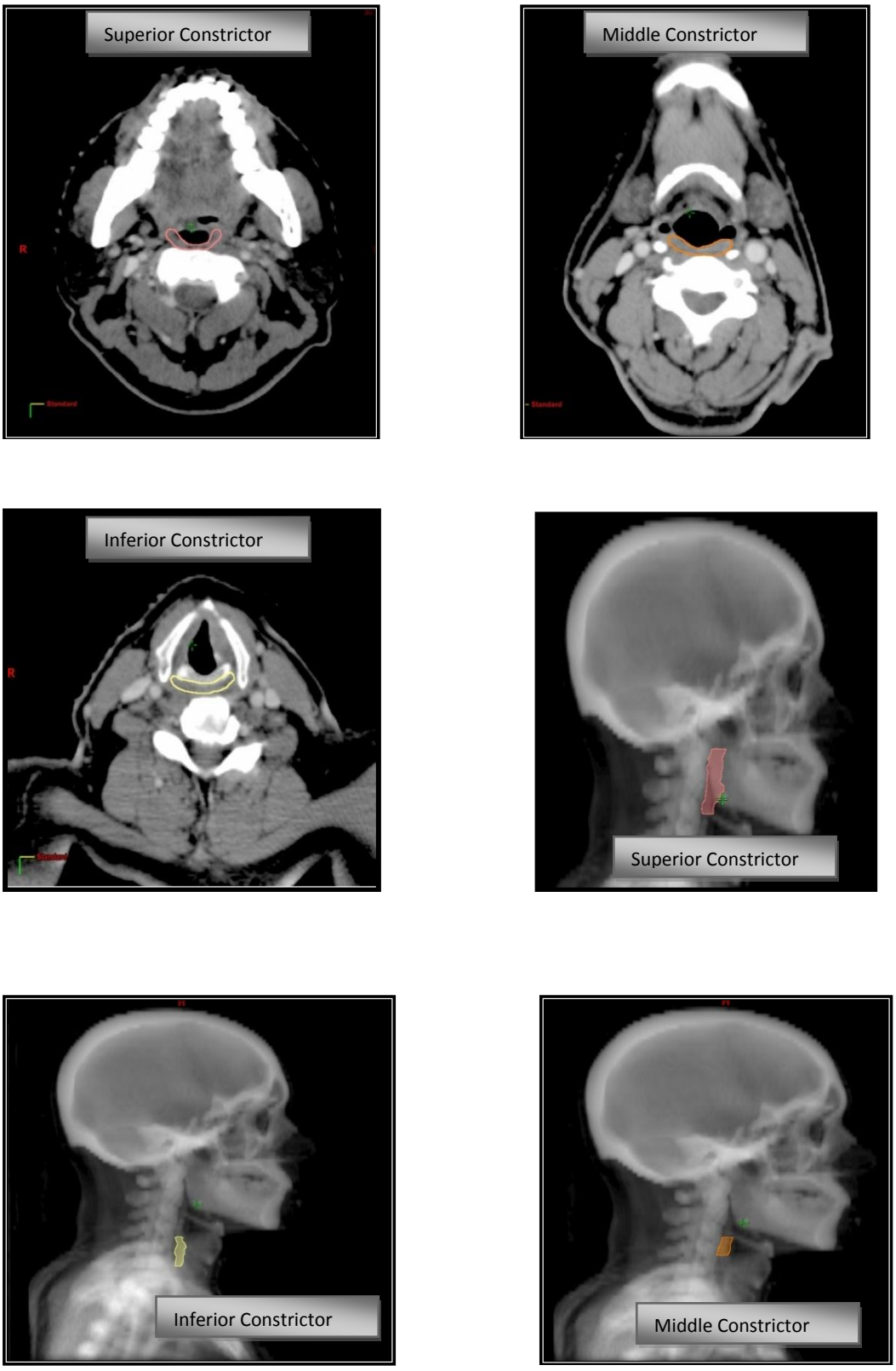


Fig: 4.1 Figure illustrates the segmentation of Superior, Middle and Inferior Constrictor muscle in axial and sagittal view.

Picture showing treatment plan

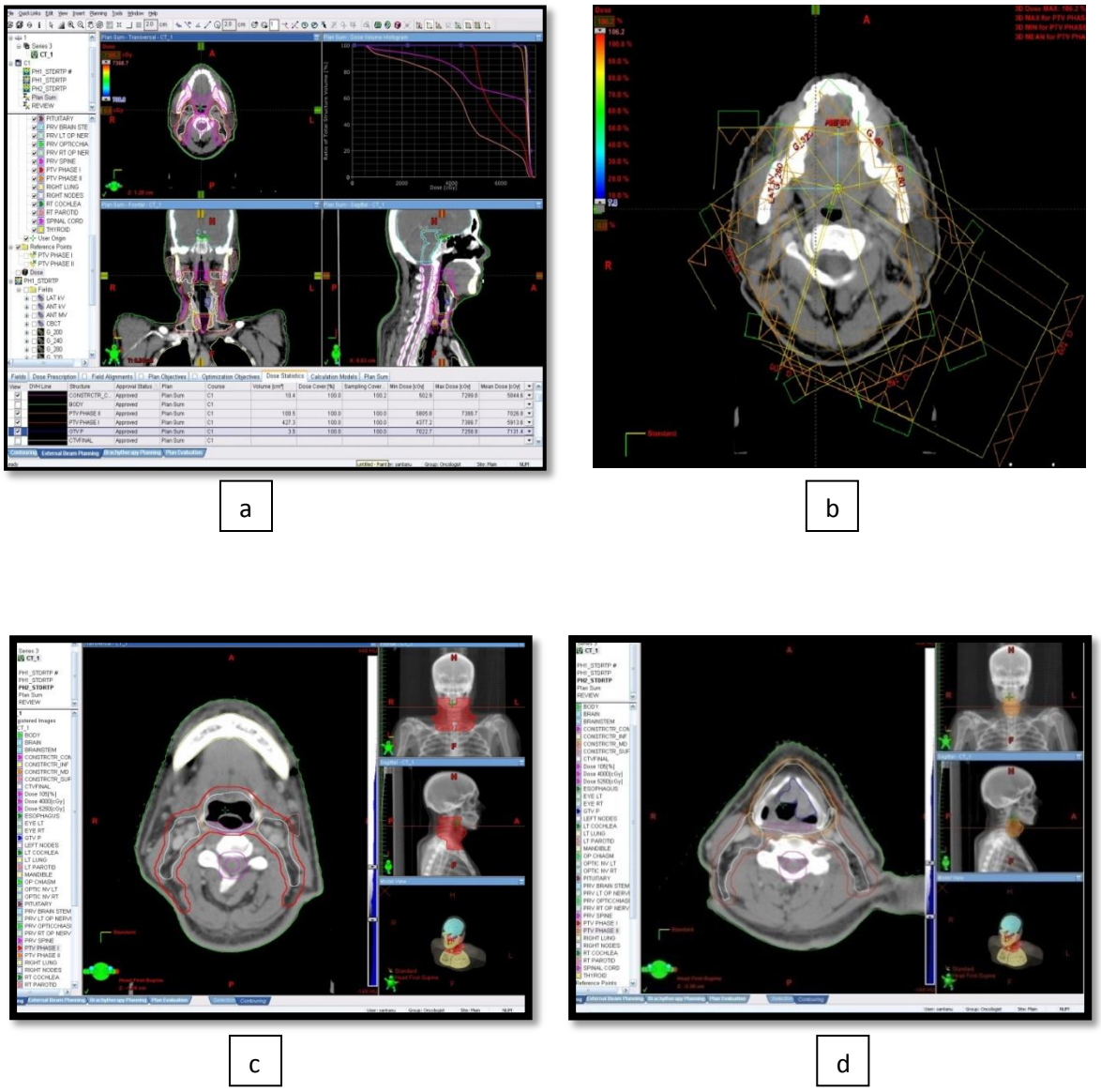
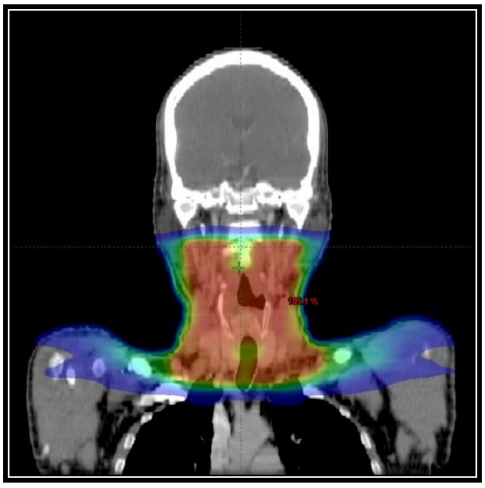


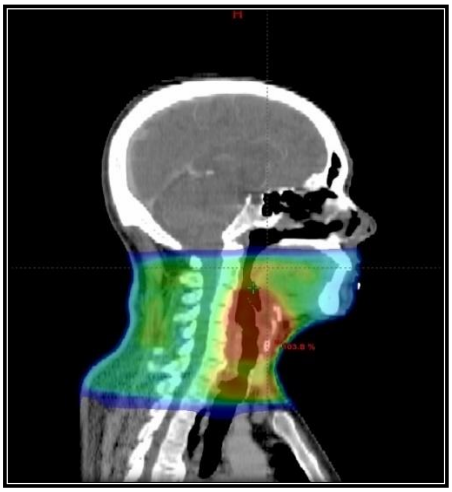
Fig. 4.2 Figure illustrates the treatment plan for a patient diagnosed with Carcinoma Supra glottis

a. Plan assessment in Planning System in different views
b. Beams arrangement view for the treatment plan
c. Phase I volume
d. Phase II volume

Picture showing dose distribution



a



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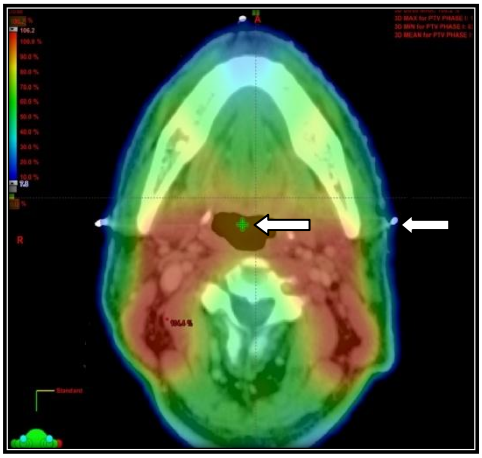

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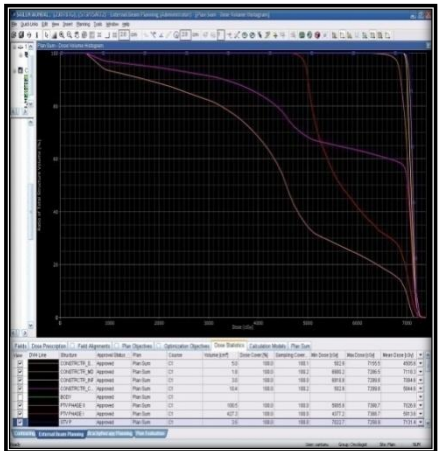


d

Fig. 4.3 Figure ilustrates plan evaluation for a patient diagnosed with Carcinoma Supra glottis

a. Dose Colour Wash in Coronal Section
b. Dose Colour Wash in Sagittal Section
c. Dose Colour Wash in Axial Section with 3 CT markers and plan isocenter
d. Cumulative Dose Volume Histogram for plan assessment

Dose prescription:

The prescribed dose was 70 Gy in 35 fractions at 2 Gy per fraction, 5 days per week, for patients with definitive intent chemo radiation therapy. Post postoperative dose prescribed was 60 Gy to 66Gy, depending upon the risk factors. In all patients, the plans addressed prescription goals as the highest priority, where as critical organ dosimetric goals (apart from spinal cord and brainstem) were considered as secondary. Optimization was done to keep minimum dose to the normal organs at risk (OARs).

Chemotherapy:

Patient received chemotherapy with Cisplatin concurrently either weekly once at dose of 40mg/m2 or three weekly once with dose of 100mg/m2.Antiemetic and pre and post chemotherapy hydration schedule were delivered according to the standard of care.(98)

Radiation therapy treatment process: (Fig 4.4)

Patients were treated with Varian CLINAC 2100 machine, from Monday through Friday. Cone beam CT was obtained for setup verification on day 1, 2, 3 and weekly once. Patients were reviewed weekly once for assessment of reactions.

Fig. 4.4 Patient treated in CLINAC for IMRT

Fig. 4.5 Flexible Naso-pharyngo-Laryngo scope used for FEES

4.4. SWALLOWING ASSESSMENT WITH MDADI QUESTIONNAIRE

Patient reported dysphagia was assessed with MDADI. Patients were asked to fill the MDADI that has 20 questions related to dysphagia before starting of radiation therapy, midway and end of radiation therapy. The 20 questions assessed 4 components like global, emotional, functional and physical aspect that reflects the Quality of life. An overall MDADI score of less than 60 represents patients having dysphagia (Bhide et al) (76) The MDADI had 3 dysphagia specific questions within MDADI Questionnaire. The 3 questions were:

P6 (Question no 7): Swallowing takes great effort

P7 (Question no10): It takes me longer to eat because of my swallowing problem

P8 (Question no 8): I cough when I try to drink liquids

The scale for the questions ranged from 1- 5, 1 representing severe complaints while 5 representing no complaints. A score of less than 3 was considered as dysphagia (according to Bhide et al)

4.5. SWALLOWING ASSESSMENT WITH FEES

Swallowing dysfunction and dysphagia were evaluated with Functional Endoscopic Evaluation of Swallowing (FEES). The FEES assessment was conducted before starting of radiation therapy as baseline. FEES were done midway during radiation therapy and end of radiation therapy. (Fig 4.5)

Patient undergoing FEES was explained in detail regarding the procedure and possible side effects. The evaluation was done in the outpatient clinic in the presence of ENT specialists, Speech therapist and Nurse. The patient was instructed to sit straight and through one nostril the Endoscope was inserted. No local anaesthesia was used.

In the first part, the assessment was done for the anatomical landmarks as the Flexible Endoscope views the nasopharynx, oropharynx and larynx. Any pooling of saliva in the valleculae or pyriform sinus was noted. The patient was instructed to vocalise a sound ‘eee’ and assessed for closure of the vocal cords.

In the second part, water mixed with edible green dye was given to the patient to swallow. Assessment of swallowing of semisolid was done with Cerelac mixture. Assessment of swallowing with the Endoscope was done with direct visualisation of the pooling of coloured liquid or food after multiple swallows.

Assessment of the swallowing was done by the combined opinion from ENT specialist and the Speech specialist. A FEES proforma based on the FEES assessment performed in NHS London was followed to document the FEES findings.

FEES assessment

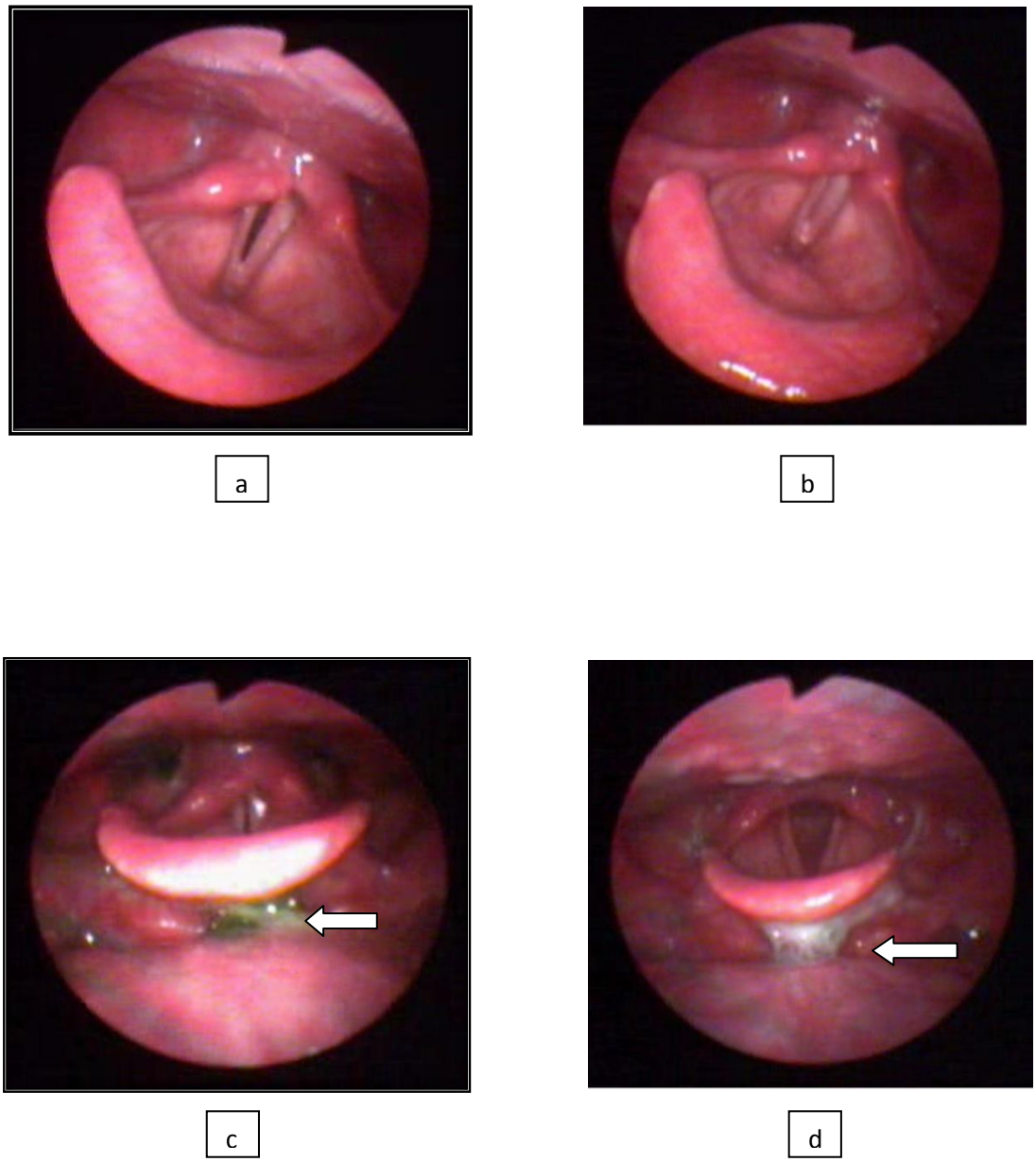


Fig. 4.4 Figure illustrates the FEES findings

a. Normal vocal cord with breathing at rest
b. Vocal cord adducted position (to assess mobility of cord)
c. Mild pooling of green coloured liquid after swallowing
d. Mild food residue after swallowing

Data collection

Treatment plans of patients were retrieved from the Eclipse planning system. The mean, maximum, and minimum doses to individual muscles and as a total combined unit were noted. Also ‘Vd’ denoting Volume in percentage receiving the dose d was obtained for each muscle and the total combined unit.

MDADI score was collected at the start of radiation therapy, midway and end of radiation therapy as shown in the Appendix. The score can range from 0 to 100, where 0 denotes severe dysphagia and 100 means no dysphagia.

FEES assessment was done with the following component

a. Anatomical assessment
b. Secretion rating (Score 0 to2, 0-normal, 2-most severe)
c. Penetration-aspiration scale(Score 1to8, 1-normal,8- most severe)
d. Consistency outcome with semi-solid and liquid (Score 0 to2, 0-normal, 2-severe)

The FEES assessment score was calculated at the start of radiation therapy, midway and end of radiation therapy as shown in the Annexure.

4.6. STATISTCAL ANALYSIS

The data from the Questionnaire, FEES assessment, and dose parameters were obtained and entered into Microsoft Excel sheet. Frequencies and percentages were calculated for the discrete variables.

For correlation between the dose to the pharyngeal constrictors and FEES assessment, patients were divided into two groups. One group had dysphagia and the other group without dysphagia, as assessed by the FEES in various ways. This was correlated to the Maximum dose and Mean dose to the pharyngeal constrictors using Wilcoxon rank sum test. For correlation between score from the questionnaire and the Maximum and Minimum doses to the pharyngeal constrictors, Pearson Correlation was used.

5. RESULTS

This study group consisted of 14 patients who underwent treatment with radiation therapy with or without chemotherapy either as the primary modality or in the postoperative setting, from March 2015 to August 2015 by IMRT technique meeting the inclusion and exclusion criteria.

The results are summarized under the following headings

1. Demographic details of the patients
2. Results of MDADI score
3. Results of FEES assessment
4. Dose characteristics to pharyngeal constrictor muscles
5. Correlation of pharyngeal constrictor dose with Dysphagia (by FEES)
6. Correlation of MDADI score with Dysphagia (by FEES)
7. Correlation of pharyngeal constrictor dose with MDADI score

5.1. DEMOGRAPHIC DETAILS OF THE PATIENTS

Distribution of patients according to age

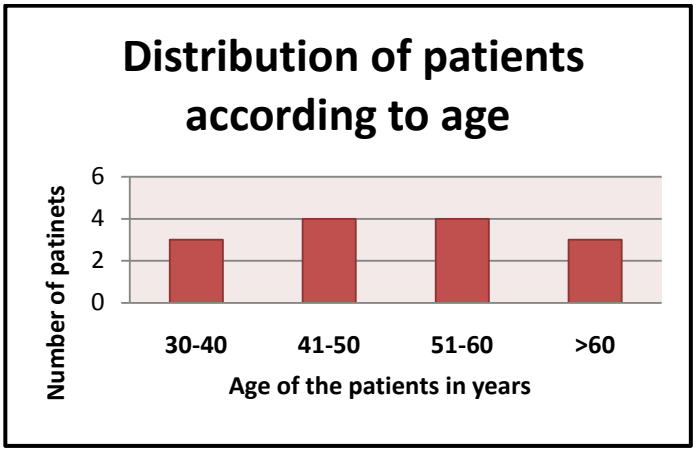


Fig 5.1.1 Histogram showing distribution of patients according to age group
Majority of the patients were in the 41 to 60 age group

Distribution of patients according to sex

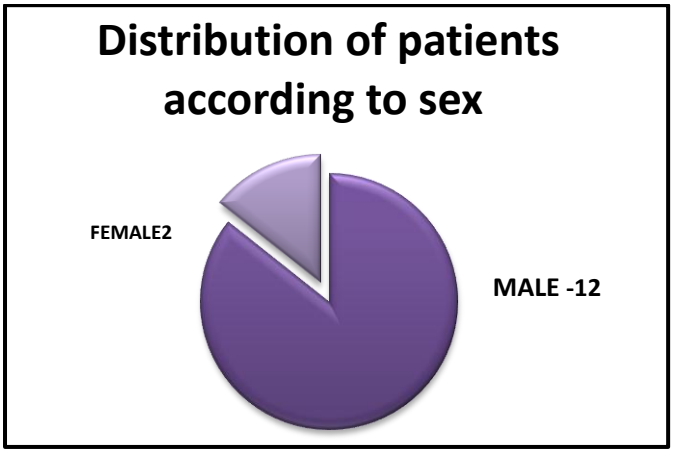


Fig 5.1.2 Pie chart showing distribution of patients according to age
Majority of the patients were males with a male to female ratio of 6:1

Distribution of patients according to different sites of cancer

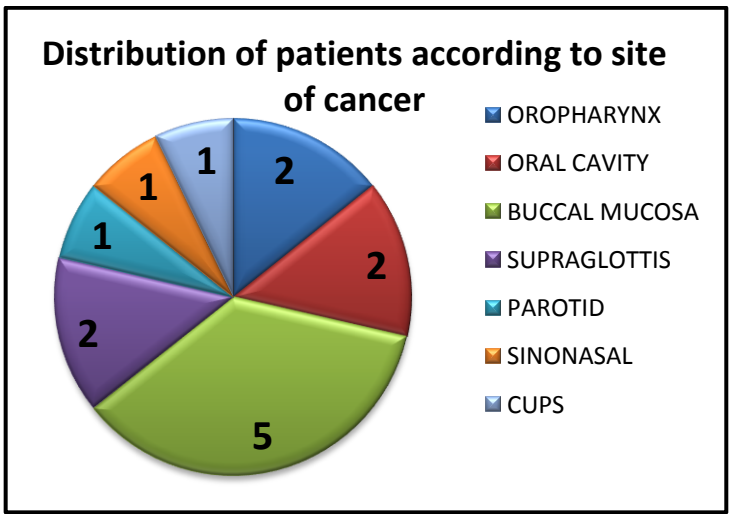


Fig 5.1.3 Pie chart showing distribution of patients according to the site of cancer
Majority of the patients included in the study had carcinoma of the buccal mucosa followed by carcinoma of the supraglottis, oral cavity and oropharynx

Distribution of patients according to the modality of treatment received

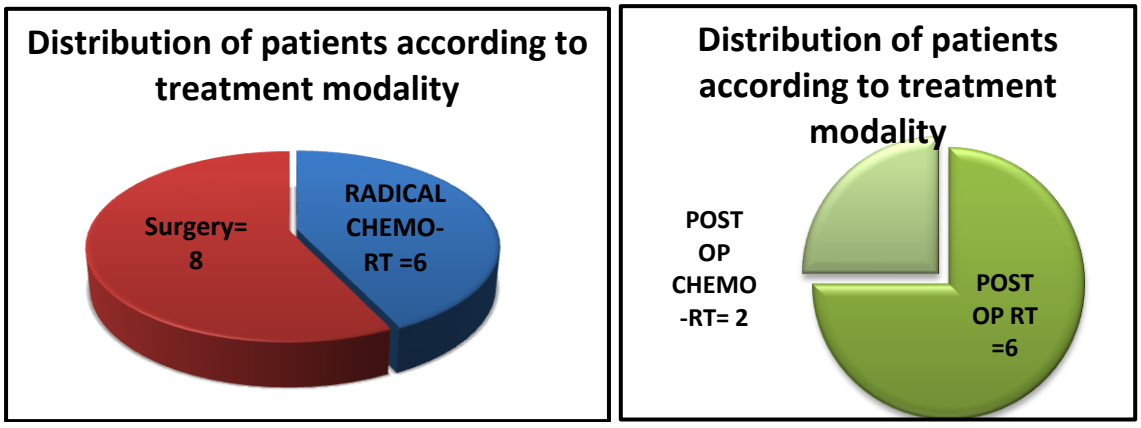


Fig: 5.1.4 Distribution of patients according to the modality of treatment received
Among the 14 patients,8 had surgery followed by appropriate post operative adjuvant radiotherapy or chemo radiation therapy and 6had definitive chemo radiation therapy. Out of the 8 patients who underwent surgery, 2 patients received chemo radiation therapy and 6 patients received only radiation therapy

Distribution of patients according to histology of the malignancy

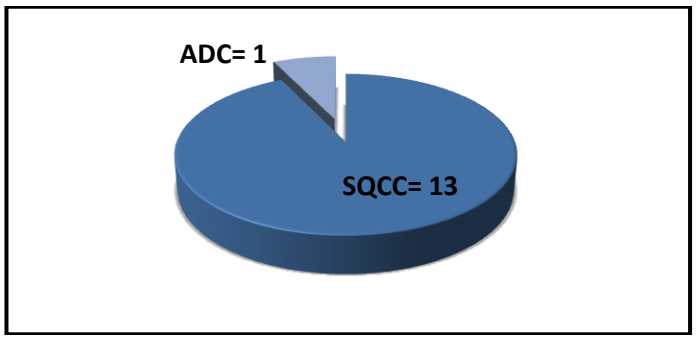


Fig 5.1.5 Pie chart showing distribution of patients according to the histology
Among the 14patients, 13 had squamous cell carcinoma (SQCC) and only1patient had adenocarcinoma (ADC).

Distribution of patients according to the dose of radiation received

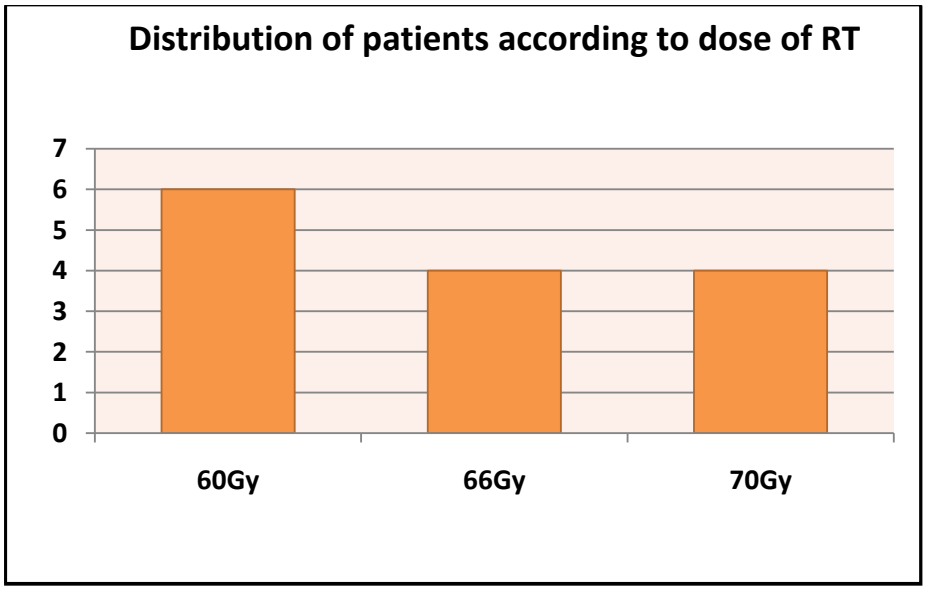


Fig 5.1.6 Distribution of the patients according to the dose of radiation received Among the 14 patients included, 6 received 60Gy and the remaining 8 received more than 66Gy.

5.2. OVERALL MDADI QESTIONNAIRE SCORE

Scores obtained from overall MDADI Questionnaire, assessed before, midway and end of radiation therapy

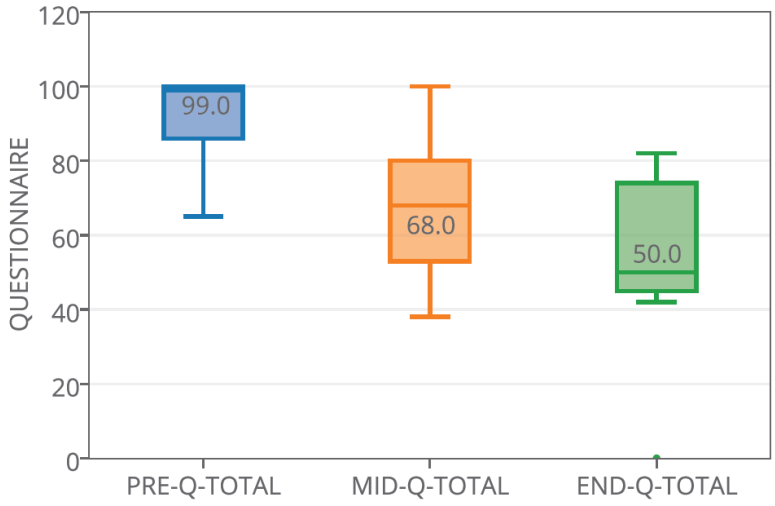


Fig 5.2.1 Box plot illustrating the overall MDADI score assessed before, midway and end of radiation therapy
The median score for all patients from the questionnaire, before radiation therapy was 99(range 65 to 100), this median score decreased to 68 (range 38 to 100) midway during radiation therapy and the score further decreased to 50 (range 42 to 82) at the end of radiation therapy.

Distribution of patients having dysphagia according to score obtained from overall MDADI questionnaire

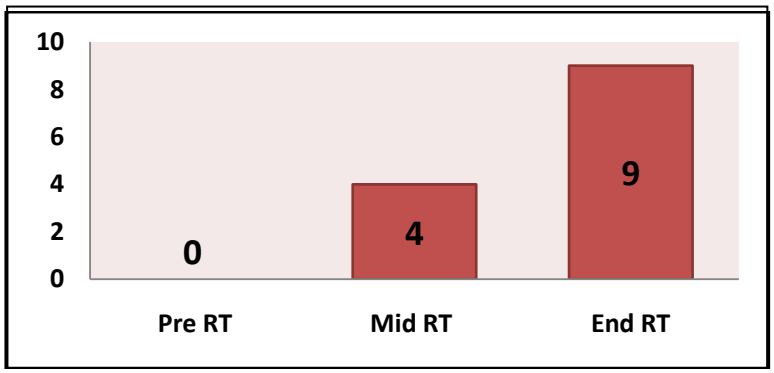


Fig 5.2.2 illustrates the distribution of patients having dysphagia according to the overall score from the MDADI questionnaire. Patients were classified as having dysphagia if the overall score from the MDADI was below 60. No patients had dysphagia prior to starting radiation therapy, 4 out of 14 patients (28%) had dysphagia midway during radiation therapy which increased to 9 out of 14 (64%) patients at the end of radiation therapy

Distribution of patients according to the score obtained from the 3 dysphagia specific questions within MDADI Questionnaire

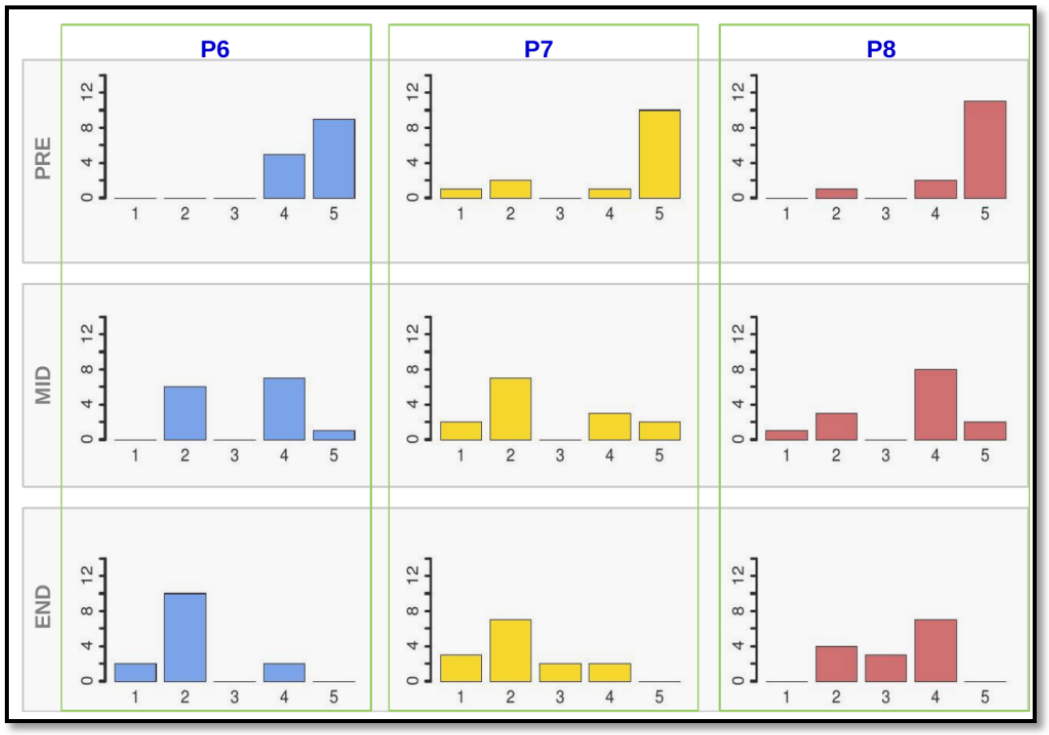


Fig 5.2.3 illustrates the distribution of patients according to the scores obtained from the3 dysphagia specific questions within MDADI Questionnaire that was assessed before, midway and end of the radiation therapy.

The 3 questions were:

P6 (Question no 7): Swallowing takes great effort

P7 (Question no10): It takes me longer to eat because of my swallowing problem

P8 (Question no 8): I cough when I try to drink liquids

The scale for the questions ranged from 1- 5, 1 representing severe complaints while 5 representing no complaints. A score of less than 3 was considered as dysphagia. For P6 (Swallowing takes great effort) all 14 patients had score of either 4 or 5 prior to starting radiation therapy. Midway during radiation therapy 42% (6/14) patients had a score of 2 (representing dysphagia) and at the end of radiation therapy 12 out of 14

(85%) patients had a score of either 1 or 2. This shows that the number of patients developing severity of dysphagia as assessed by the question P6 (swallowing takes great effort) increased with increasing doses of radiation and this occurred in 42% (6/14) of patients midway and increased to 85% (12/14) by end of radiotherapy.

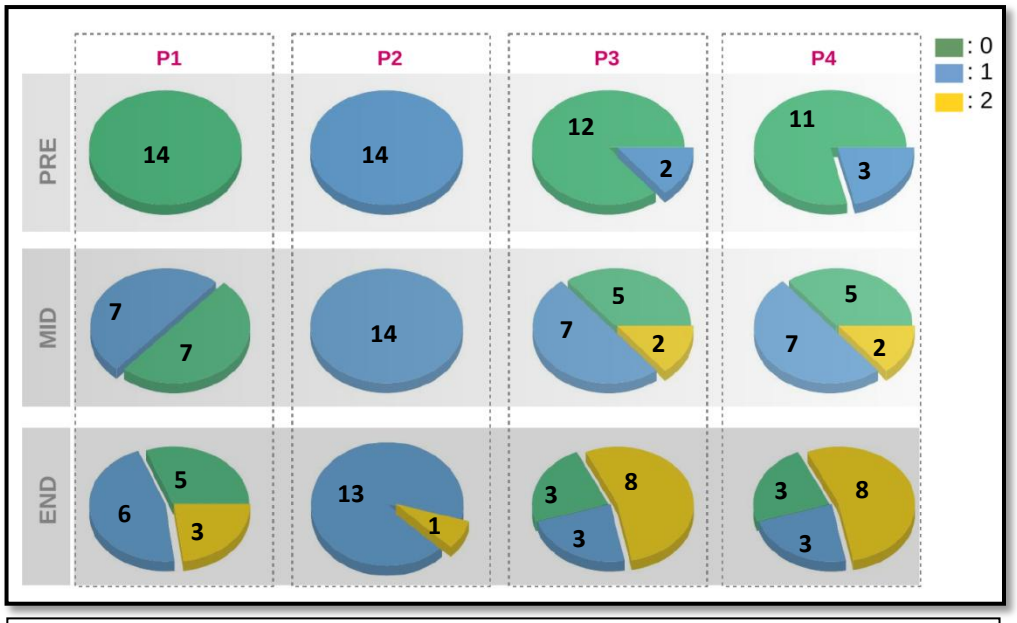
For P7 (It takes me longer to eat because of my swallowing problem) majority- 78% (11/14) of the patients had a score of 4 or 5 and 21% (3/14) had a score of 1 or 2prior to starting of radiation therapy.

Midway during radiation therapy 9 out of 14 (64%) had a score of either 1 or 2 and at the end of radiation therapy 10 out of 14 (71%) had a score of either 1 or 2. This shows that majority(64% - 9/14) of patients developed severity of dysphagia as assessed by the question P7 (It takes me longer to eat because of my swallowing problem) by midway of radiation therapy and only 1 more by end of radiation therapy (71% - 10/14).

For P8 (I cough when I try to drink liquids) only 8% (1/14) patient had a score less than 3, rest 92% (13/14) had a score of either 4 or 5 prior to starting radiation therapy. 28% (4/14) had a score less than 3 mid way during radiation therapy and 50% (7/14) had a score of less than 3 at the end of radiation therapy. This shows the number of patients developing severity of dysphagia as assessed by the question P8 (I cough when I try to drink liquids) increases with increasing doses of radiation and this occurred in 28% (4/14) of patients midway and increased to 50% (7/14) by end of radiation therapy.

5.3. FEES ASSESSMENT:

Distribution of patients according to the findings in FEES assessed before, midway and at the end of radiation therapy.



Colour – represents the scale/severity of dysphagia, for P2 (Penetration Aspiration scale) none had scored more than 2, hence none colour code shown

Area of the Pie represents number of patients with dysphagia

Fig 5.3.1 Figure illustrates the results of the FEES assessment with 4 ways for the assessment of dysphagia. They were as follows:
P1- Secretion rating (range 0- 2, 2=severe problems)
P2-Penetration-aspiration scale (range 1-8, 8=severe problems)
P3-Swallowing with liquid (range 0- 2, 2=severe problems)
P4-Swallowing with semisolid (range 0- 2, 2=severe problems)

For P1 (assessment with secretion rating) none had dysphagia prior to starting of radiation therapy, 50% (7/14) had mild dysphagia (score 1) midway during radiation therapy and at the end of radiation therapy 42% (6/14) had mild dysphagia (score 1) and 21% (3/14) had severe dysphagia (score 2).

For P2 (assessment with penetration aspiration scale) none had dysphagia prior to starting of radiation therapy or midway during radiation therapy. 1 out of 14 had score 2 at the end of Radiation therapy (score 2 indicates –food material enters airway, remains above the vocal folds and is ejected out from the airway)

For P3 and P4 (assessment with swallowing for liquids and semisolids) 2 out of 14 patients had mild dysphagia for liquids prior to starting of radiation therapy (score 1) and 3 out of 14 patients had mild dysphagia for semi solids prior to starting of radiation therapy(score of 1).

Midway during radiation therapy, 50% (7/14) of the patients had mild dysphagia for both liquids and semisolids (score 1), and this included the 2 patients who had mild dysphagia, prior to starting radiation therapy. 14% (2/14) of the patients had severe dysphagia for both liquids and semisolids (score 2) and these 2 patients had no abnormality (score 0) prior to starting radiation therapy. Rest 36% (5/14) had no problems with swallowing.

At the end of radiation therapy, 21% (3/14) of the patients had mild dysphagia for both liquids and semisolids (score 1), while 57% (8/14) of the patients had severe dysphagia for both liquids and semisolids (score 2). Remaining 21% (3/14) of the patients had no problems at the end of radiation therapy.

5.4. DOSIMETRIC CHARACTERISTICS

Volume of the pharyngeal constrictor muscles and dose received

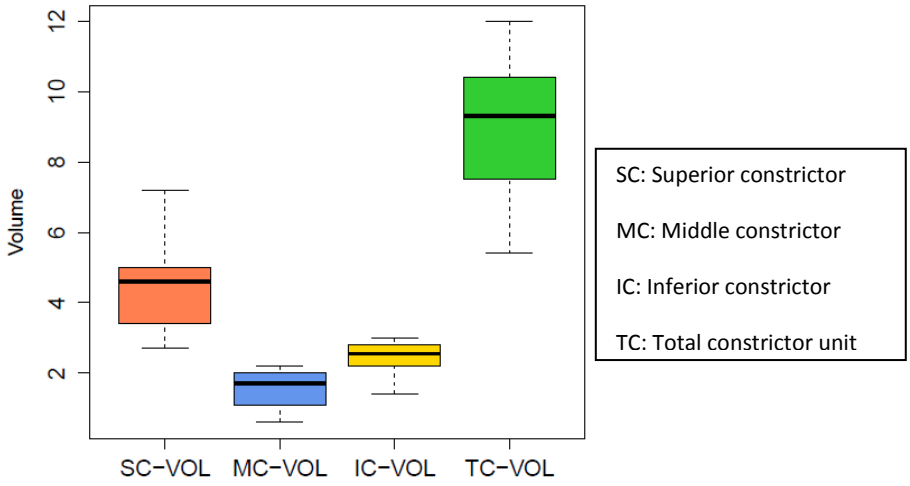


Fig 5.4.1 Box plots that illustrates the volume of the pharyngeal constrictor muscles for all patients segmented for the treatment

For all patients, the volume of Superior constrictor muscle ranged from 2.7cc to 7.2cc with a median of 4.6cc. The volume varied according to the length of the neck of each patient. For Middle constrictor, the volume of muscle receiving dose for all patients ranged from 0.6cc to 2.2cc with a median of 1.7cc. For Inferior constrictor, the volume of muscle receiving dose for all patients ranged from 1.4cc to 3cc with a median of 2.55cc. For Total constrictor unit, the volume of muscle receiving dose for all patients ranged from 5.4cc to 12cc with a median of 9.3 cc. This shows that there is more variation in the volume of the superior constrictor depending on the length of the neck, as compared to the middle and inferior constrictor.

Radiation therapy dose received by individual muscles during radiation therapy
Superior Constrictor Muscle dose

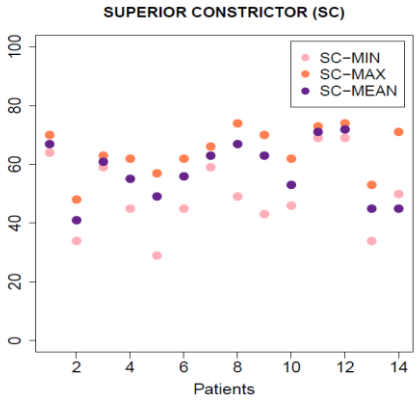


Fig 5.4.2 Fig shows the minimum, mean and maximum doses to superior constrictor muscles for all patients. The dose to superior constrictor was minimum of 29 Gy and maximum of 74 Gy. The mean dose to superior constrictor was minimum of 41Gy and maximum 72Gy

Middle Constrictor Muscle dose

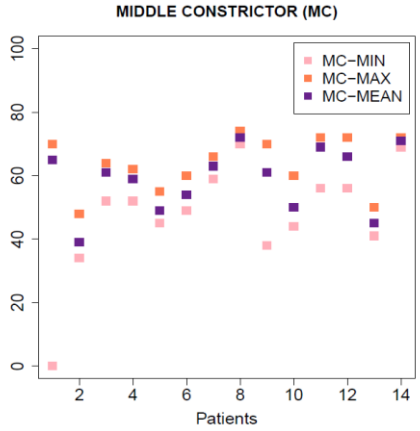


Fig 5.4.3 Fig shows minimum, mean and maximum doses to middle constrictor muscles for all patients. The dose to middle constrictor was minimum of 0 Gy and maximum of 74 Gy. The mean dose to middle constrictor was minimum of 39 Gy and maximum of 72 Gy.

Inferior Constrictor Muscle dose

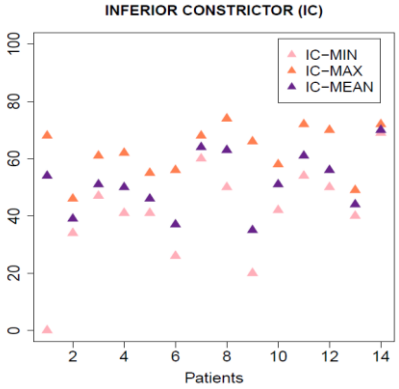


Fig 5.4.4 Fig shows minimum, mean and maximum doses to middle constrictor muscles for all patients. The dose to inferior constrictor was minimum of 0 Gy and maximum of 74 Gy. The mean dose to superior constrictor was minimum of 37 Gy and maximum of 72Gy.

Distribution of radiation doses received by pharyngeal constrictor muscles according to the site of malignancy

Diagram showing the Maximum doses to each respective pharyngeal constrictor muscle and total combined unit according to site of cancer

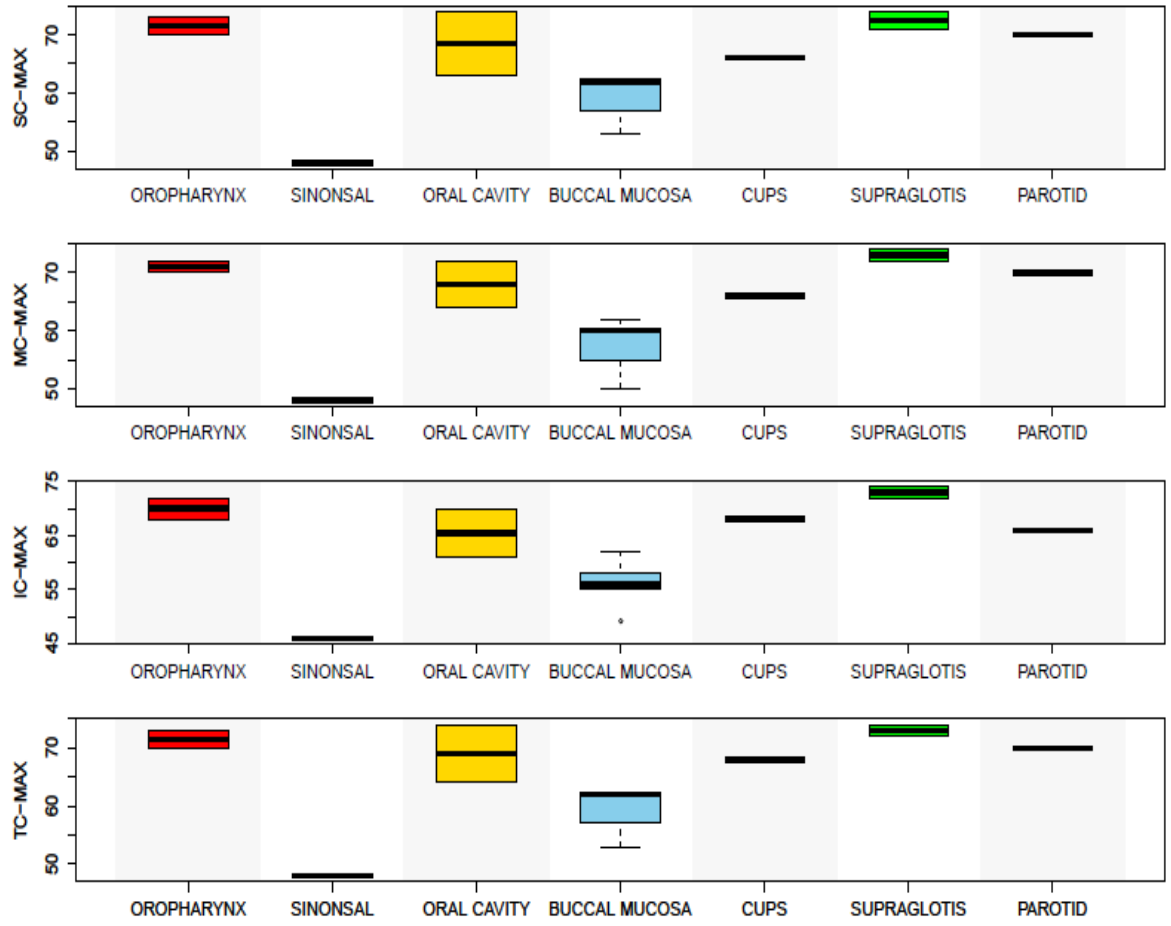


Fig 5.4.5 Figure shows Maximum doses to constrictor muscles for all patients according to the site of malignancy

For patients with sinonasal carcinoma and buccal mucosa the median value of the maximum doses to all pharyngeal constrictors was below 60 Gy. For oropharyngeal carcinoma, oral cavity and supraglottis, the median value of maximum doses to all the pharyngeal constrictors was more than 60 Gy.

Diagram showing the mean doses to each respective pharyngeal constrictor muscle and total combined unit according to site of cancer

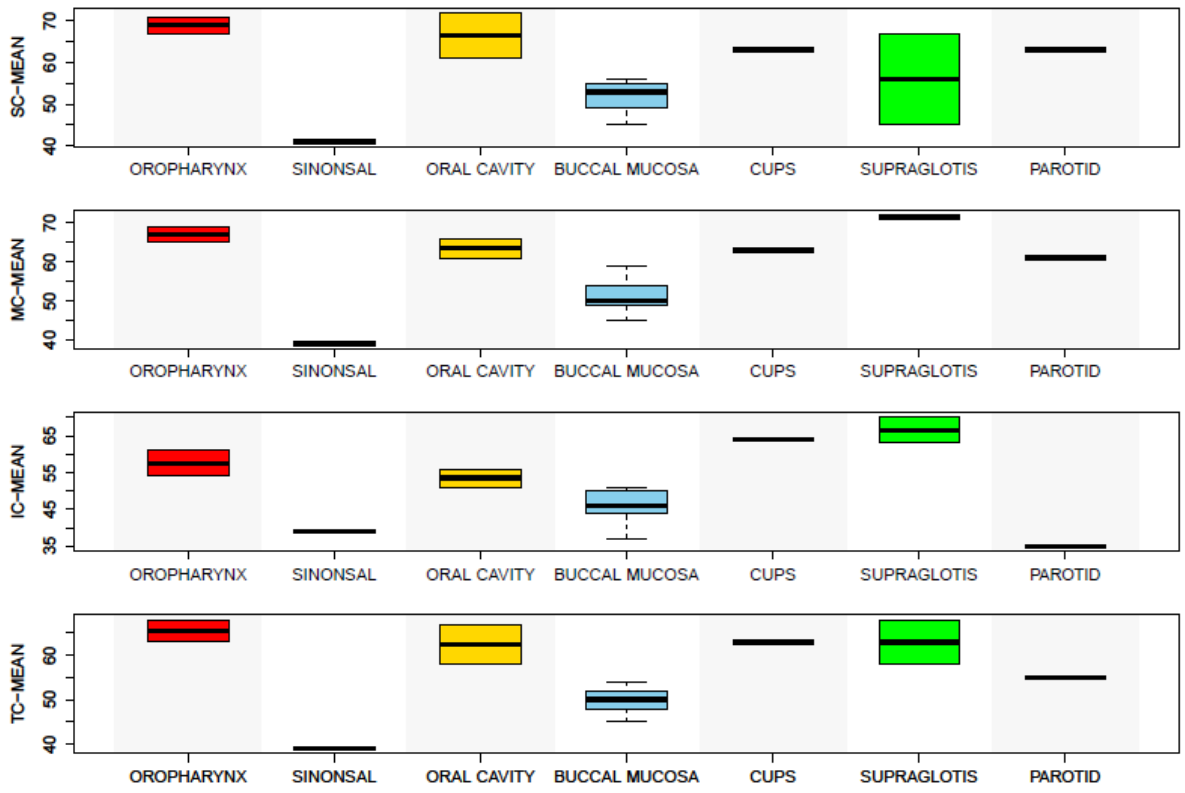


Fig 5.4.6 Figure shows Mean doses to constrictor muscles for all patients according to the site of malignancy.

For sinonasal carcinoma and buccal mucosa the median value of the mean dose to pharyngeal constrictors was below 55Gy. For oropharyngeal carcinoma, oral cavity and supraglottis, the median value of mean doses to all the pharyngeal constrictors was more than 55Gy.

Diagram showing the V_{10} to V_{70} for each of the pharyngeal constrictors

SUPERIOR CONSTRICTOR V_{10} TO V_{70}

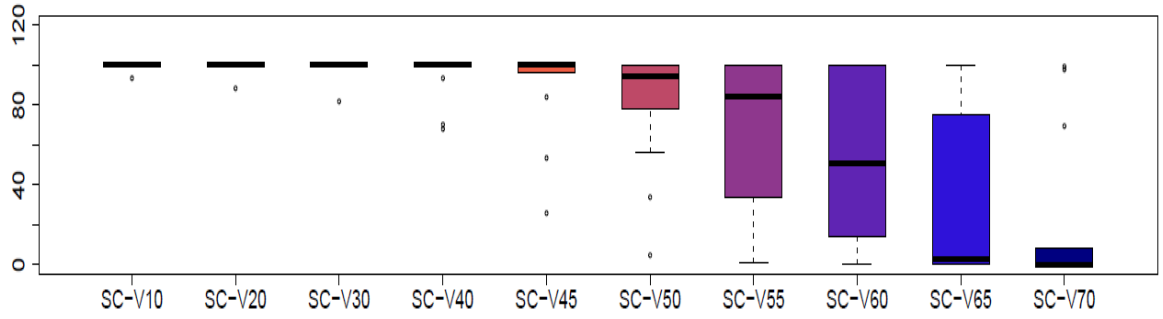


Fig 5.4.7 Fig illustrates the Volume (%) of the SC receiving dose'd'. The median V_{50} is almost 100% for all patients. The median V_d gradually decreases with increase in dose 'd', as seen from median V_{55} (90%) to median V_{70} (0%).

MIDDLE CONSTRICTOR V_{10} TO V_{70}

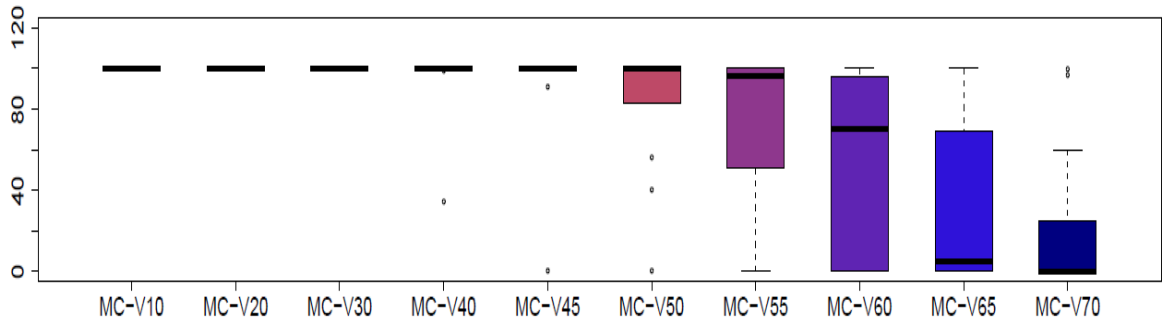


Fig 5.4.8 Fig illustrates Volume (%) of the MC receiving dose'd'. The median V_{50} is almost 100% for all patients. The median V_d gradually decreases with increase in dose'd', as seen from median V_{60} (70%) to median V_{70} (0%)

INFERIOR CONSTRICTOR V_{10} TO V_{70}

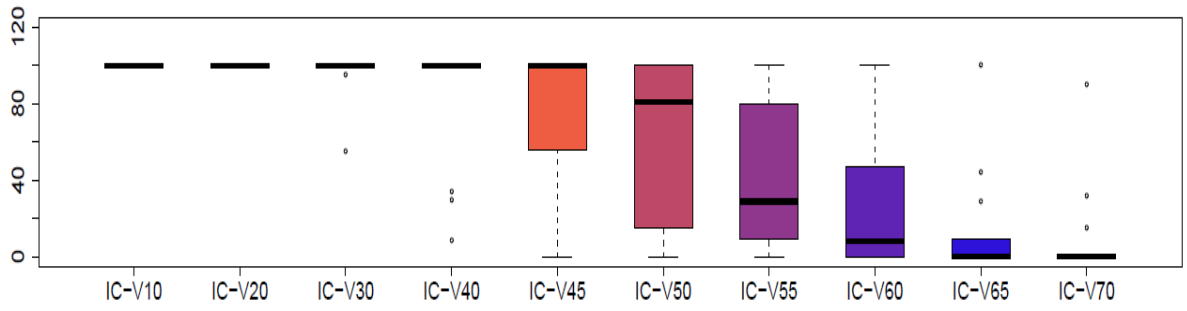


Fig 5.4.9 Fig illustrates the Volume (%) of the IC receiving dose'd'. The median V_{45} is almost 100% for all patients. The median V_d gradually decreases with increase in dose 'd', as seen from median V_{50} (80%) to median V_{70} (0%)

TOTAL CONSTRICTOR UNIT V_{10} TO V_{70}

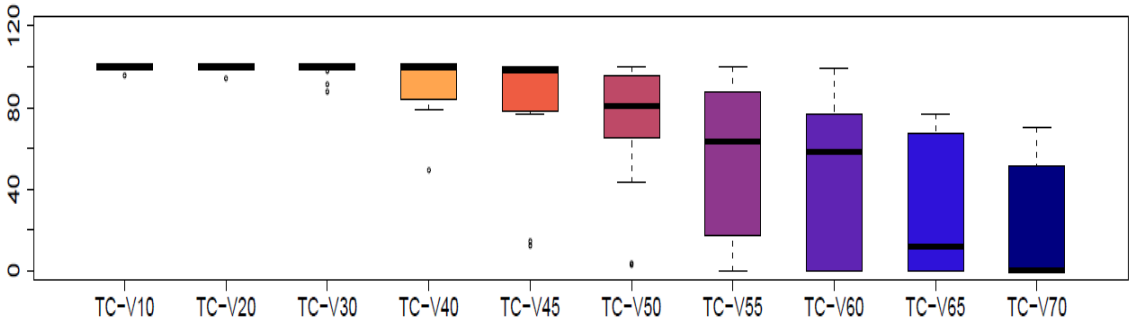


Fig 5.4.10 Fig illustrates the Volume (%) of the TC receiving dose'd'. The median V_{45} is almost 100% for all patients. The median V_d gradually decreases with increase in 'd', as seen from median V_{50} (80%) to median V_{70} (0%)

5.5. CORRELATION OF DOSE WITH DYSPHAGIA (Assessed by FEES)

In the diagrams below, Y axis show the dose to the respective pharyngeal constrictor muscles and X axis show patients with and without dysphagia (blue –no dysphagia and green –dysphagia). P- Value signifies the statistical significance.

Diagram to show correlation between maximum dose to each of the pharyngeal constrictor muscles and dysphagia at the end of radiation therapy (assessed by swallowing liquids and semisolids in FEES, P3 and P4)

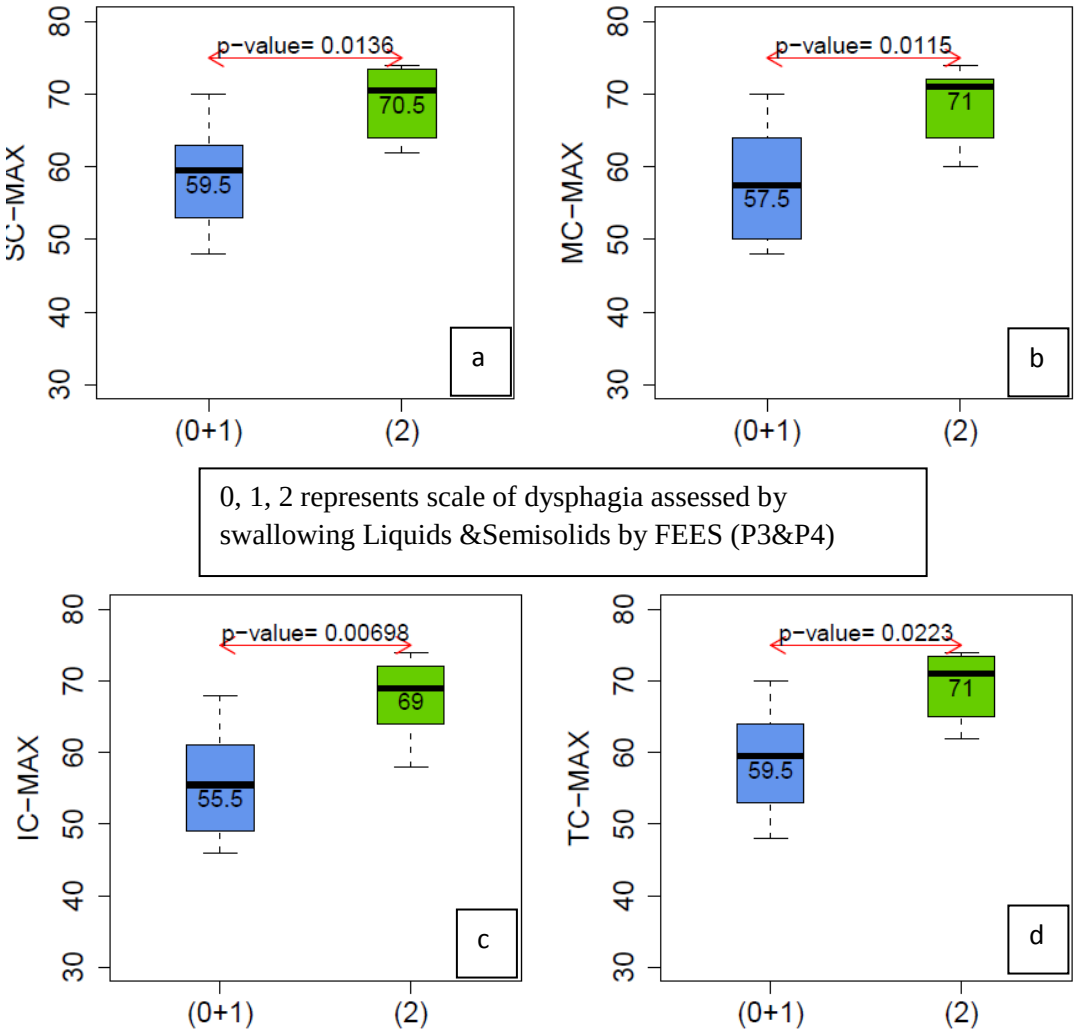


Fig 5.5 figure illustrating the correlation with **maximum doses** to Pharyngeal constrictor muscles and dysphagia as assessed by **swallowing liquids and semisolids by FEES (P3) and (P4)**

In fig 5.5.a the maximum doses to Superior Constrictor in the group of patients with dysphagia (score of 2) ranged from 62Gy to 74Gy with a median dose of 70.5 Gy, while maximum dose to SC in the group of patients without dysphagia (score of 0, 1) ranged from 48Gy to 70Gy with a median dose of 59.5 Gy. When the median dose to SC between the two groups (with and without dysphagia) was compared, there was a difference with statistical significance (p=0.01).

In fig 5.5.b the maximum doses to Middle Constrictor in the group of patients with dysphagia (score of 2) ranged from 60 Gy to 74 Gy with a median dose of 71 Gy, while maximum dose to MC in the group of patients without dysphagia (score of 0, 1) ranged from 48Gy to 70Gy with a median dose of 57.5 Gy. When the median dose to MC between the two groups (with and without dysphagia) was compared, there was a difference with statistical significance (p=0.01).

In fig 5.5.c the maximum doses to Inferior Constrictor in the group of patients with dysphagia (score of 2) ranged from 58 Gy to 74 Gy with a median dose of 69 Gy, while maximum dose to IC in the group of patients without dysphagia (score of 0, 1) ranged from 46 Gy to 68Gy with a median dose of 55.5 Gy. When the median dose to IC between the two groups (with and without dysphagia) was compared, there was a difference with statistical significance (p=0.006).

In fig 5.5.d the maximum doses to Total Constrictor unit in the group of patients with dysphagia (score of 2) ranged from 62 Gy to 74 Gy with a median dose of 71 Gy, while maximum dose to IC in the group of patients without dysphagia (score of 0, 1) ranged from 48 Gy to 70 Gy with a median dose of 59.5 Gy. When the median dose to IC between the two groups (with and without dysphagia) was compared, there was a difference with statistical significance ($p=0.02$)

Similar analysis was also done by comparing the median value of the maximum doses between the group with dysphagia (score 1, 2) and without dysphagia (score of 0). Results showed no statistical significance between the two groups

Analysis was done by comparing maximum dose to each of the pharyngeal constrictor muscles and dysphagia at the end of radiation therapy (assessed by Secretion Rating of FEES, P1) Results showed no statistical significance between the two groups

Diagram to show correlation between MEAN dose to each of the pharyngeal constrictor muscles and dysphagia at the end of radiation therapy (assessed by swallowing liquids and semisolids in FEES, P3 and P4)

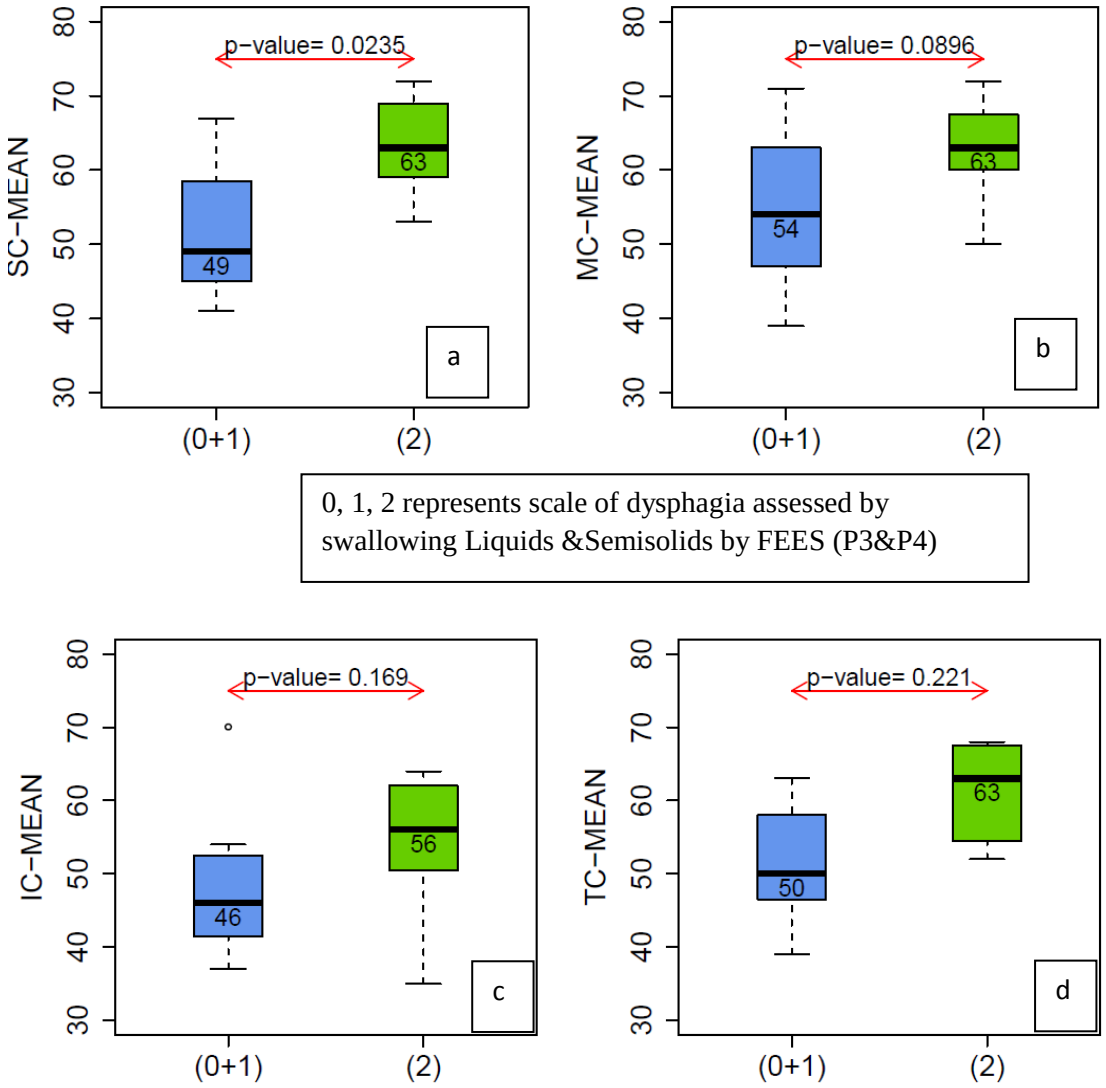


Fig 5.6 Figure illustrating the correlation with **mean doses** to Pharyngeal constrictor muscles and dysphagia as assessed by **swallowing liquids and semisolids by FEES (P3) and (P4)**

In fig 5.6.a the Mean doses to Superior Constrictor in the group of patients with dysphagia (score of 2) ranged from 53 Gy to 72 Gy with a median dose of 63 Gy, while Mean dose to SC in the group of patients without dysphagia (score of 0, 1) ranged from 41Gy to 67 Gy with a median dose of 49 Gy. When the median dose to SC between the two groups (with and without dysphagia) was compared, there was difference and with statistical significance (p=0.02).

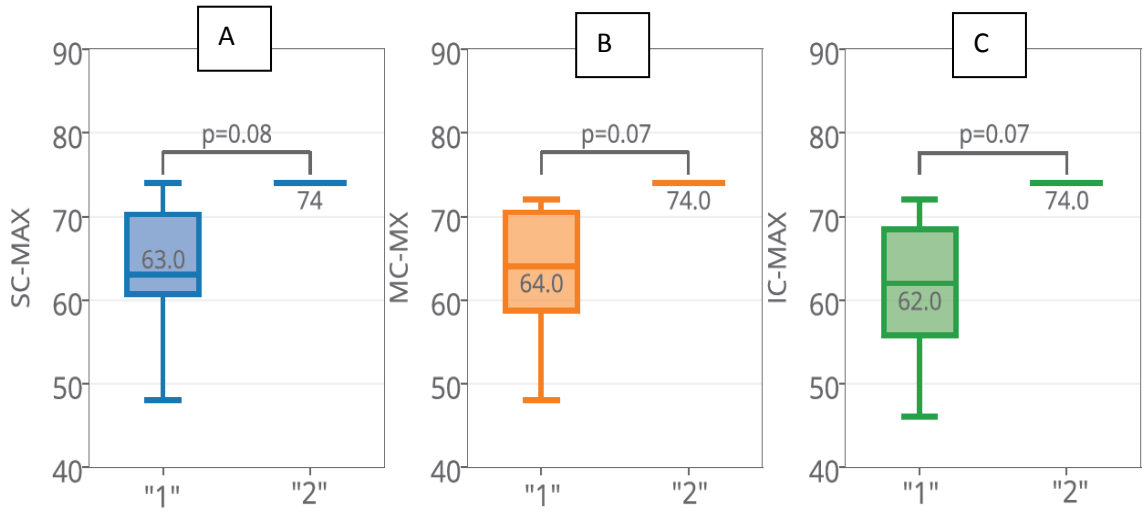
In fig 5.6.b the Mean doses to Middle Constrictor in the group of patients with dysphagia (score of 2) ranged from 50 Gy to 72 Gy with a median dose of 63 Gy, while Mean dose to MC in the group of patients without dysphagia (score of 0, 1) ranged from 39 Gy to 71 Gy with a median dose of 54 Gy. When the median dose to MC between the two groups (with and without dysphagia) was compared, there was no difference and no statistical significance (p=0.17).

In fig 5.6.c the Mean doses to Inferior Constrictor in the group of patients with dysphagia (score of 2) ranged from 35 Gy to 64 Gy with a median dose of 56 Gy, while Mean dose to IC in the group of patients without dysphagia (score of 0, 1) ranged from 36 Gy to 55 Gy with a median dose of 46 Gy. When the median dose to IC between the two groups (with and without dysphagia) was compared, there was no difference and no statistical significance (p=0.16).

In fig 5.6.d the Mean doses to Total Constrictor unit in the group of patients with dysphagia (score of 2) ranged from 52Gy to 67 Gy with a median dose of 63 Gy, while Mean dose to TC in the group of patients without dysphagia (score of 0, 1) ranged from 39 Gy to 62 Gy with a median dose of 50 Gy. When the median dose to IC between the two groups (with and without dysphagia) was compared, there was a no difference with no statistical significance (p=0.22)

Similar analysis was also done by comparing the median value of the Mean dose between the group with dysphagia (score 1, 2) and without dysphagia (score of 0). Results showed no statistical significance between the two groups.

Diagram to show correlation between Maximum dose to each of the pharyngeal constrictor muscles and dysphagia at the end of radiation therapy (assessed by penetration and aspiration scale in FEES, P2



1, 2 represents scale of dysphagia assessed by penetration aspiration scale by FEES (P2) No patients had score more than 2. (Scale range 1to 8)

Fig 5.7 Figure illustrating the correlation with **Maximum doses** to Pharyngeal constrictor muscles and dysphagia as assessed according **to Penetration- aspiration scale FEES (P2).**

Only 1 out of 14 patients had a score of 2 when assessed by FEES with penetration aspiration scale. (Score 2 represents food material enters the airway, remains above the vocal folds and is ejected from the airway). No patients had scored more than 2 on assessment with FEES.

In fig 5.7.a the Maximum dose to Superior Constrictor in the patients with dysphagia (score of 2) was 74 Gy, while Maximum dose to SC in the group of patients with score of 1) ranged from 48 Gy to 74 Gy with a median dose of 63 Gy. When the median dose to SC between the two groups was compared, there was no difference and no statistical significance (p=0.08).

In fig 5.7.b the Maximum dose to Middle Constrictor in the patient with dysphagia (score of 2) was 74 Gy, while Maximum dose to MC in the group of patients with score of 1) ranged from 48 Gy to 72 Gy with a median dose of 64 Gy. When the median dose to MC between the two groups was compared, there was no difference and no statistical significance (p=0.07).

In fig 5.7.c the Maximum dose to Inferior Constrictor in the patient with dysphagia (score of 2) was 74 Gy, while Maximum dose to IC in the group of patients with score of 1) ranged from 46 Gy to 72 Gy with a median dose of 62 Gy. When the median dose to IC between the two groups was compared, there was no difference and no statistical significance (p=0.07)

Therefore no results showed statistical significant (p >0.05) for Maximum dose to Superior constrictor, Middle constrictor, inferior constrictor.

Diagram to show the correlation of V_d (Volume in percent receiving the dose 'd') for Superior Constrictor muscle and dysphagia as assessed by Swallowing LIQUID & SEMISOLIDS by FEES (P3) and (P4)

In the diagrams below – Y axis show the Volume receiving dose D (V_d) for respective pharyngeal constrictor muscles and X axis – two groups in two colours (blue –no dysphagia and green –dysphagia). P- Value signifies the statistical significance.

SUPERIOR CONSTRICTOR

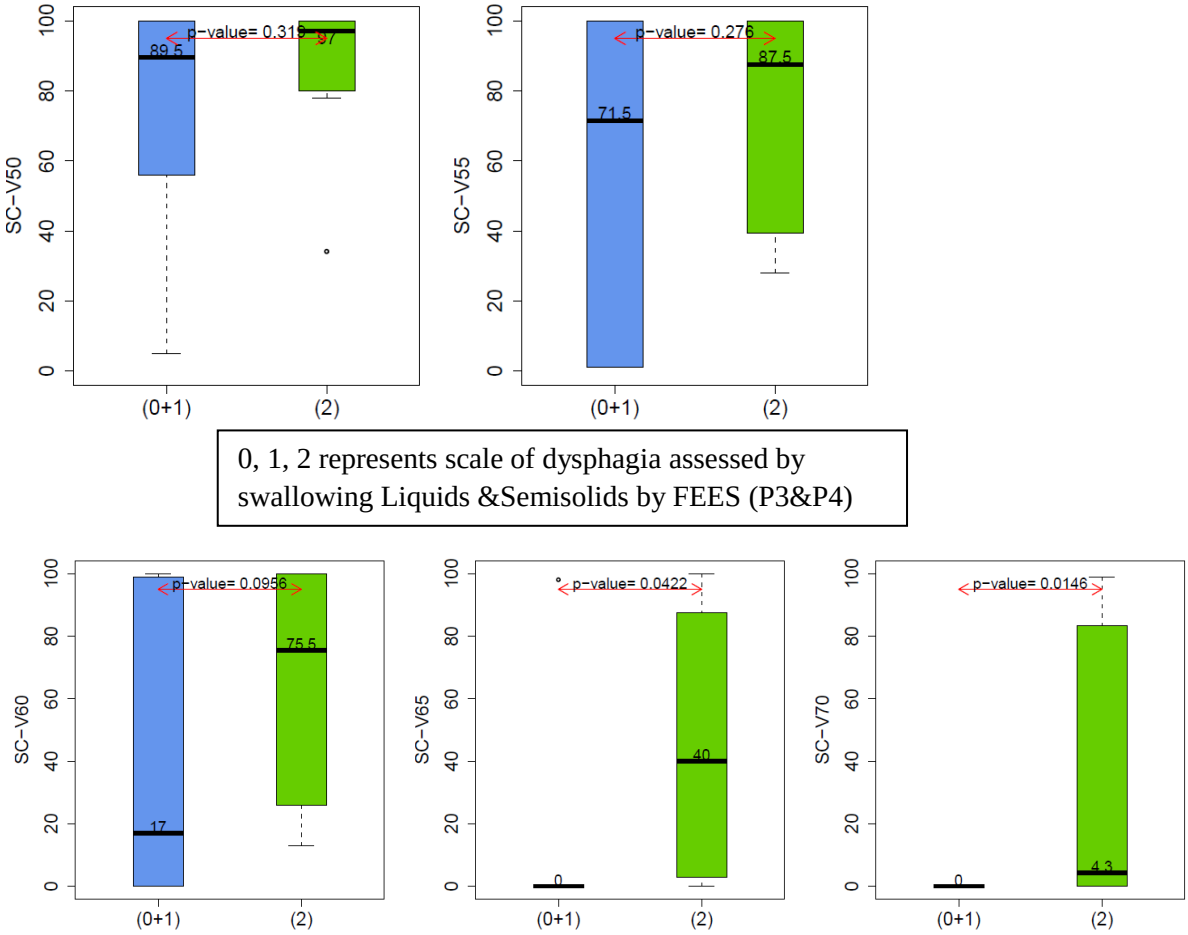


Fig 5.8 Figure illustrating the correlation with **V_d of Superior Constrictor** muscle and dysphagia as assessed by **Swallowing LIQUID & SEMISOLIDS by FEES (P3) and (P4).**

The median volume (in percent) receiving dose'd' in patients with dysphagia (score 2, as assessed by swallowing liquids or semisolids in FEES) was compared to the median volume (in percent) receiving the same dose'd' in patients without dysphagia (score 0,1 assessed by FEES).The Figure shows that in V_{65} and V_{70}, i.e. the Volume receiving dose 65 Gy and 70 Gy respectively was higher in the patients with dysphagia compared to the other group and this was also statistically significant. **Statistical significant (p <0.05) for Superior constrictor V_{65} and V_{70}.**

MIDDLE CONSTRICTOR

Diagram to show the correlation of V_d (Volume in percent receiving the dose'd') for Middle Constrictor and dysphagia as assessed by Swallowing LIQUID & SEMISOLIDS by FEES (P3) and (P4)

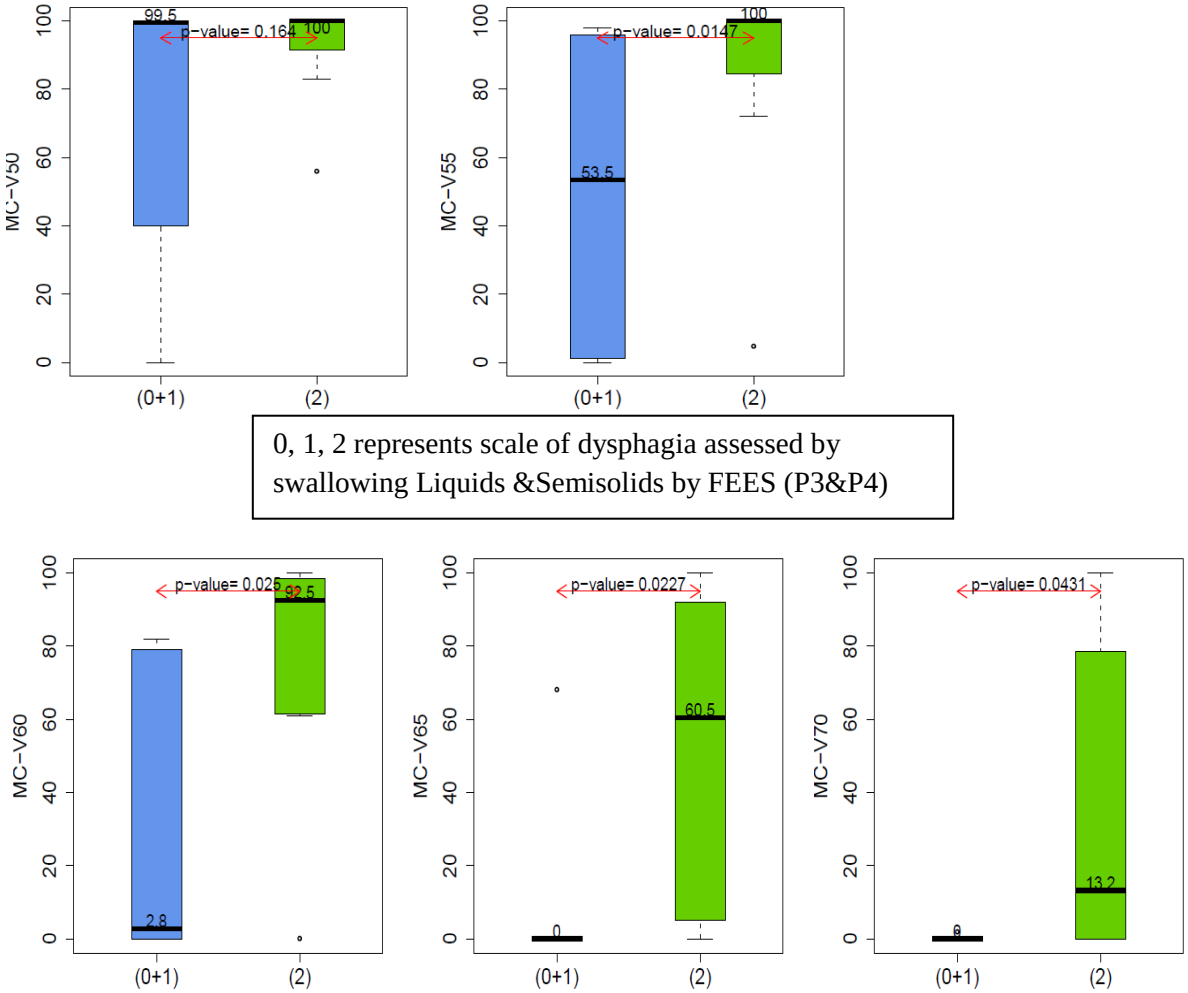


Fig 5.9 Figure illustrating the correlation with **V_d of Middle Constrictor** and dysphagia as assessed by **Swallowing LIQUID & SEMISOLIDS by FEES (P3) and (P4).**

The median volume (in percent) receiving dose'd' in patients with dysphagia (score 2, as assessed by swallowing liquids or semisolids in FEES) was compared to the median volume (in percent) receiving the same dose'd' in patients without dysphagia (score 0,1asessed by FEES) The Figure shows that in V_{55} V_{60} V_{65} and V_{70}, i.e. the Volume(in percent) receiving dose 55 Gy, 60 Gy, 65 Gy and 70 Gy respectively was higher in the patients with dysphagia compared to the other group , that were also statistically significant ($p<0.05$) in all the above mentioned figures.

INFERIOR CONSTRICTOR

Diagram to show the correlation of V_d (Volume in percent receiving the dose'd') for Inferior Constrictor and dysphagia as assessed by Swallowing LIQUID & SEMISOLIDS by FEES (P3) and (P4)

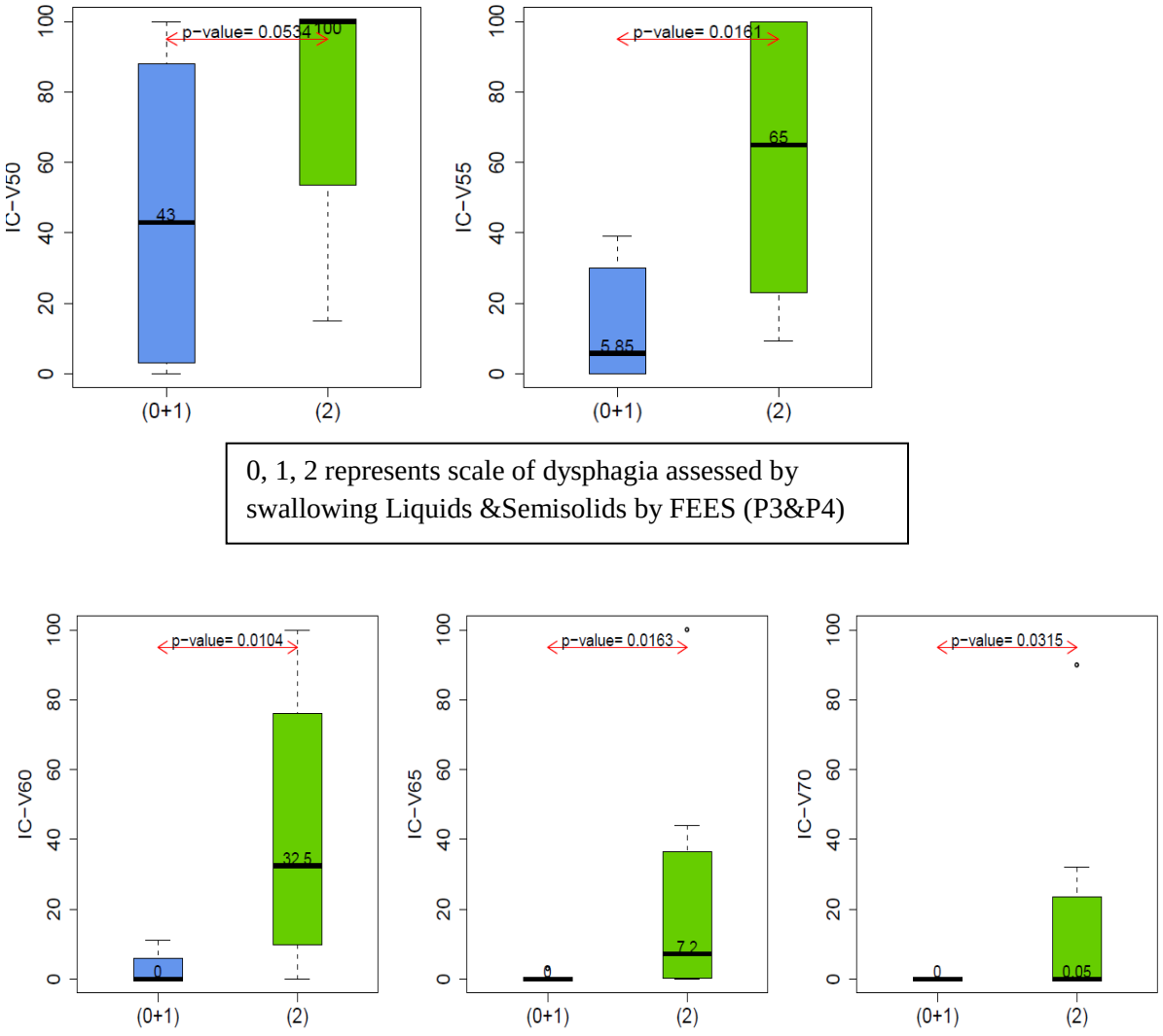


Fig 5.10 Figure illustrating the correlation with **V_d of Inferior Constrictor** and dysphagia as assessed by **Swallowing LIQUID & SEMISOLIDS by FEES (P3) and (P4).**

The median volume (in percent) receiving dose'd' in patients with dysphagia (score 2, as assessed by swallowing liquids or semisolids in FEES) was compared to the median volume (in percent) receiving the same dose'd' in patients without dysphagia (score 0,1asessed by FEES). The Figure shows that in V_{50},V_{55}, V_{60} ,V_{65} and V_{70}, i.e the Volume (in percent) receiving dose 50 Gy, 55 Gy, 60 Gy, 65 Gy and 70 Gy respectively was higher in the patients with dysphagia compared to the other group , that were also statistically significant ($p<0.05$) in all the above mentioned figures.

5.6. CORRELATION OF MDADI SCORE WITH DYSPHAGIA (assessed by FEES)

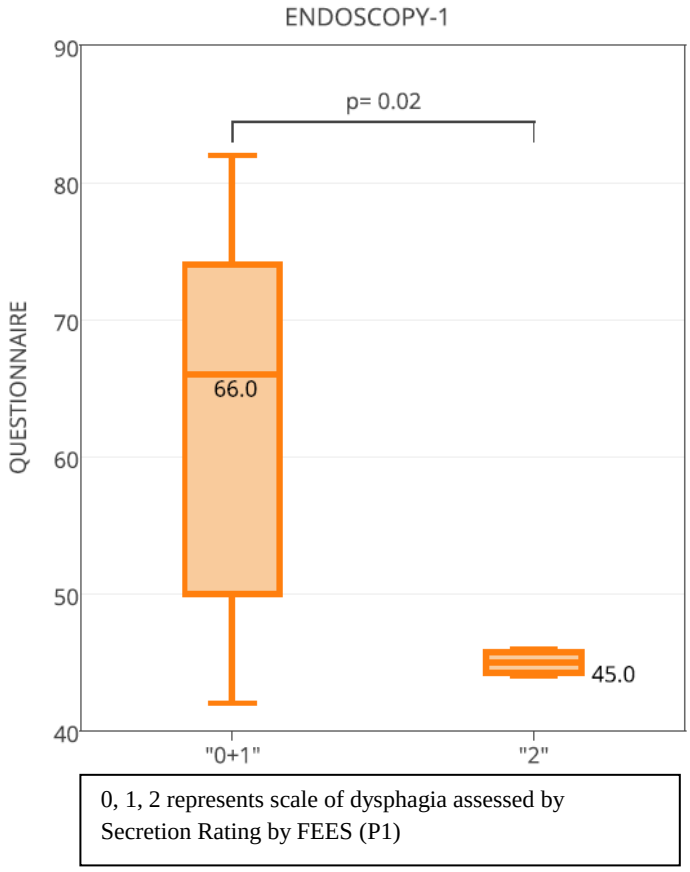


Fig 5.6.1 Figure illustrating the correlation with **MDADI** score assessed at the end of radiation therapy and **dysphagia** as assessed by **Secretion Rating by FEES (P1).**

Patients who had dysphagia (score of 2, as assessed with secretion rating in FEES) had MDADI score ranged from 44 to 46 with median score of 45. Patients who had no dysphagia (score of 0, 1 as assessed with secretion rating in FEES) had MDADI score ranged from 42 to 82 with median score of 66. When the median score between the two groups were compared there was difference that was statistical significant with p value of 0.02. This shows that patients who had dysphagia (assessed by FEES) also reported poor quality of life with MDADI score below 60.

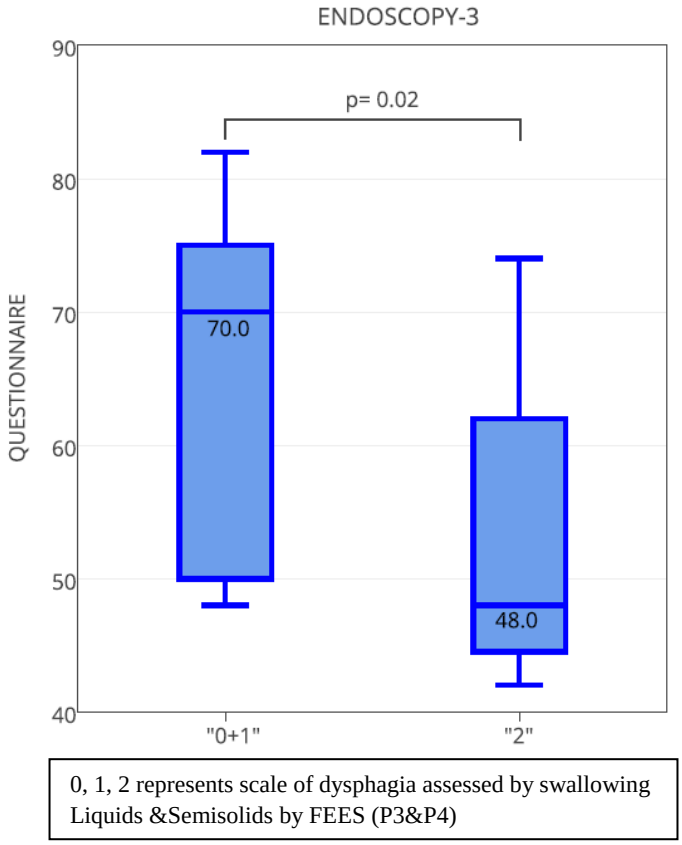


Fig 5.6.2 Figure illustrating the correlation with **MDADI Questionnaire** score assessed at the end of radiation therapy and **dysphagia** assessed by **Swallowing LIQUID & SEMISOLIDS by FEES (P3) and (P4)**

Patients who had dysphagia (score of 2, as assessed with swallowing liquid and semisolid in FEES) had MDADI score ranged from 42 to 74 with median score of 48. Patients who had no dysphagia (score of 0, 1 as assessed swallowing liquid and semisolid in FEES) had MDADI score ranged from 48 to 75 with median score of 70. When the median score between the two groups were compared there was difference that was statistical significant with p value of 0.02. This shows that patients who had dysphagia (assessed by FEES) also reported poor quality of life with MDADI score below 60.

5.7. CORRELATION OF MDADI QUESTIONNAIRE WITH DOSE TO PHARYNGEAL CONSTRICTORS

Correlation of MDADI score with dose to Superior Constrictor

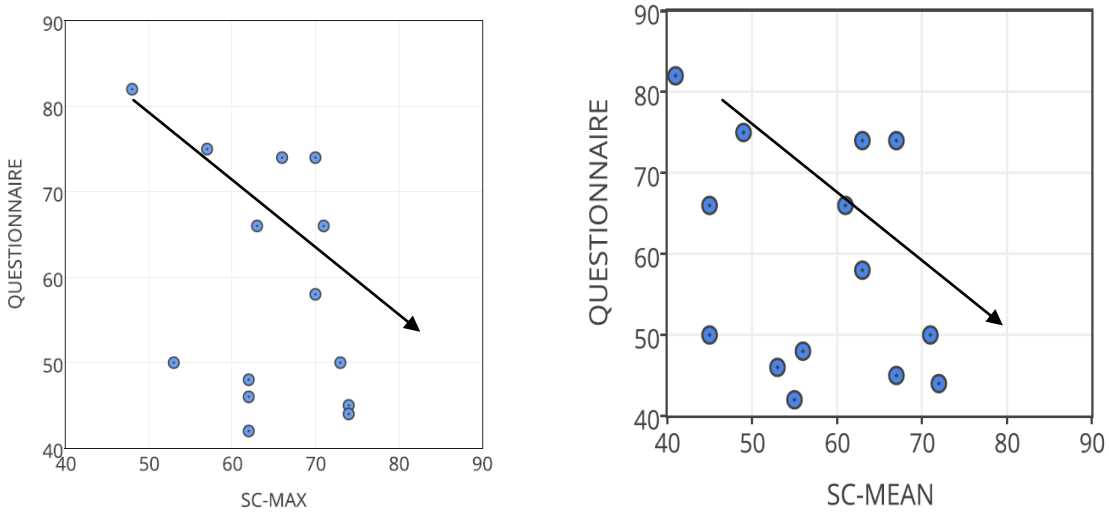


Fig 5.7.1 Figure illustrating the correlation with **MDADI** score assessed at the end of radiation therapy and **Maximum and Mean doses to the Superior constrictor muscle.** In both the above figures it can be seen that with the increase in Maximum and Mean doses to the SC, there was worsening of the MDADI scores. These figures represent the negative correlation, and show that with increase in doses to the muscle there is decrease in MDADI scores.

Correlation of MDADI score with dose to Middle Constrictor

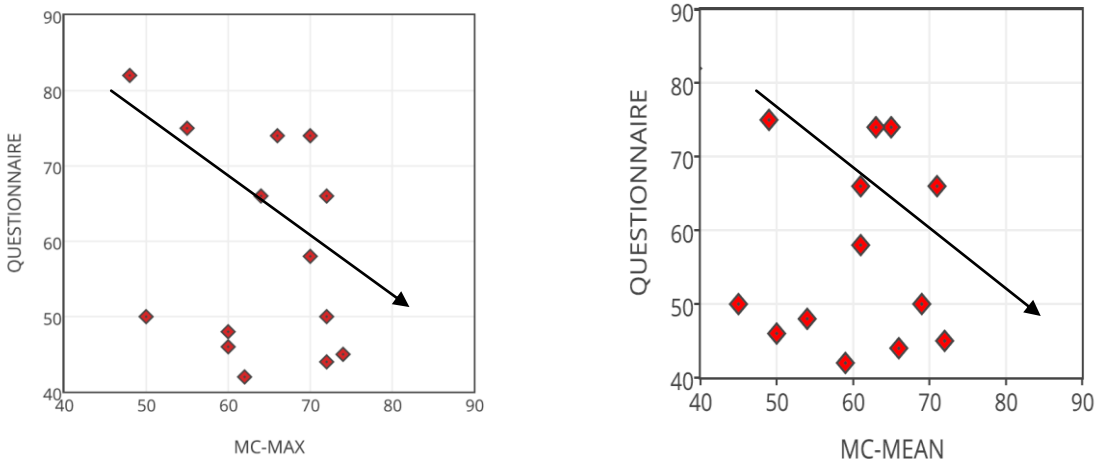


Fig 5.7.2 Figure illustrating the correlation with **MDADI**score assessed at the end of radiation therapy and **Maximum and Mean dose to the Middle constrictor muscle.**
In both the above figures it can be seen that with the increase in Maximum and Mean doses to the MC, there was worsening of the MDADI scores. These represent the negative correlation, and show that with increase in doses to the muscle there is decrease in MDADI scores

Correlation of MDADI score with dose to Inferior Constrictor

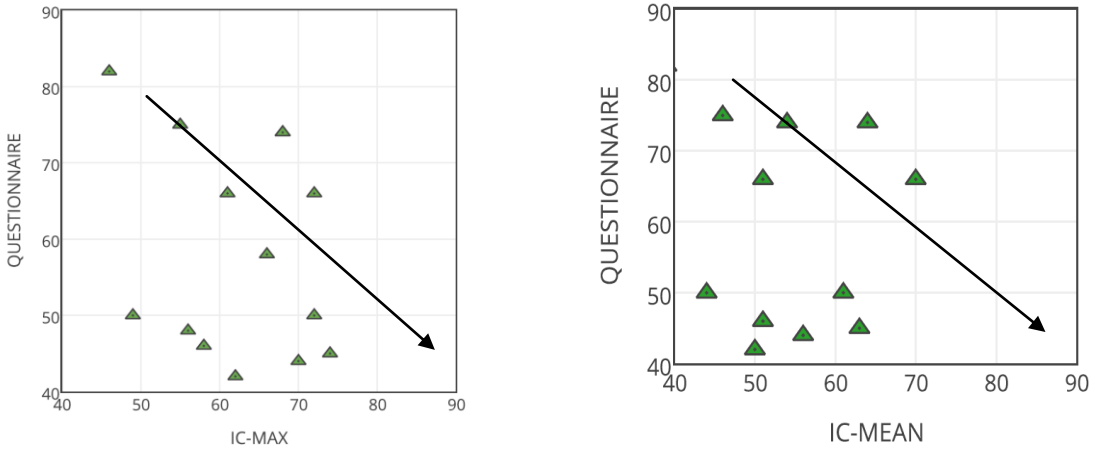


Fig 5.7.3 Figure illustrating the correlation with **MDADI Questionnaire** score assessed at the end of radiation therapy and **Maximum and Mean dose to the Inferior constrictor muscle**

In both the above figures it can be seen that with the increase in Maximum and Mean doses to the IC, there was worsening of the MDADI scores. These represent the negative correlation, and show that with increase in doses to the muscle there is decrease in MDADI scores

6. DISCUSSION

Radiation therapy is one of the main modalities of treatment for head and neck cancers either alone or in combination with chemotherapy or surgery. Patients undergoing radiation therapy can have significant problems during and post treatment in the form of mucositis, xerostomia and dysphagia which affects their quality of life. Although IMRT can help in reducing dose to the salivary glands and reduce xerostomia and dysphagia, its role in preventing dysphagia by reducing dose to pharyngeal structures and constrictor muscles is controversial.

This study was conducted therefore in a prospective manner and aimed to assess the correlation between the radiation dose to the pharyngeal constrictors with subjective and objective assessment of swallowing function in patients with head and neck cancer undergoing treatment with radiation therapy with IMRT technique. At present in view of time constraints, results and analysis have been conducted based on acute findings (mid and end of Radiation therapy assessment). Long term follow up to assess the late changes in dysphagia observed following radiation therapy should be undertaken.

In this study the majority of the study population were in the age group of 41 years to 60 years and the male to female ration was 6:1. Among the 14 patients 8 had radiation therapy in the adjuvant setting and other 6 had definitive radiation therapy. Majority of the patients (8 out of 14) received radiation dose more than 60 Gy.

All patients in our study had no complaints of dysphagia and no radiological involvement of pharyngeal constrictors prior to radiation therapy.

According to the study by Bhide et al.(76), MDADI score below 60 reflected poor quality of life related to dysphagia. Similar findings were also noted in our study, where 4 patients had MDADI score less than 60 midway during radiation therapy and 9 patients at the end of radiation therapy. This reflects the impact of dysphagia in quality of life in patients with head and neck cancers, during radiation therapy.

The same above mentioned author also studied the correlation between various MDADI scores (like Global score, physical score, emotional score and dysphagia specific scores) and the objectively assessed grade of dysphagia. In his study there was a significant correlation between MDADI score and grade of dysphagia which was also seen in our study. The patients in our study were also assessed with FEES and classified into two groups. It was found that those patients, who were assessed to have significant dysphagia by FEES, also had low MDADI score reflecting poor QoL due to dysphagia.

Feng et al study (69)(71) showed that patient reported swallowing function was significantly associated with the mean pharyngeal constrictor dose and among the pharyngeal constrictors, superior constrictor had the highest correlation. In our study similar correlation was seen with the superior constrictors only.

It was also observed that there was a correlation between patient reported MDADI score and the maximum dose and mean dose to all the constrictors, similar to the study by Feng et al. It was noted in our study that with increase in maximum or mean dose

to pharyngeal constrictor muscles there was worsening of quality of life due to dysphagia as reflected by the worsening MDADI score. However, in our study none of these correlations were statistically significant and this may be due to small number of patients included.

Also, in the study by Feng et al, all patients who developed aspiration by video fluoro scopy (VFS) were found to have mean dose to the pharyngeal constrictor muscles above 60Gy. A study by Jensen et al on 35 patients with VFS showed that mean dose less than 60Gy resulted in low risk of aspiration. In contrast to the above studies, Bhide et al and Laan et al(99) concluded that the exact relationship between the radiation doses to the constrictor and post radiotherapy dysphagia is still unclear.

In our study the correlation between the dose to the pharyngeal constrictors and dysphagia was assessed by FEES. Patients who developed severe dysphagia (as assessed by swallowing liquids and semisolids) had a higher mean dose to superior constrictor muscle that was statistically significant.

In addition to this, our study also showed that patients who had dysphagia also had a higher maximum dose to all the pharyngeal constrictors (SC, MC and IC) which was statistically significant.

According to Anderson et al study (75) that validated the Quantec recommendations showed that V_{50} less than 30% resulted in decreased acute toxicity of Grade 3 dysphagia. Our study showed that patients, who had dysphagia assessed by FEES, had V_{65} more than 40% for superior constrictor, V_{65} more than 60% for middle constrictor and V_{55} more than 50% for inferior constrictor.

LIMITATION

The study population was small with 14 patients. More number of patients would help in better statistical analysis to correlate the dose and dysphagia assessment.

A significant number of patients had surgery, followed by adjuvant radiation therapy. These patients were included as they did not have complaints of dysphagia and fulfilled all other inclusion criteria. But on analysis this group were found to have poor oral phase of swallowing on FEES that might affect the overall swallowing function and therefore these patients should be looked at separately.

During radiation therapy patients often develop mucositis as a part of treatment. This can affect the assessment with MDADI questionnaire. Follow up assessments with the same questionnaire can help to distinguish between mucositis and dysphagia.

7. CONCLUSION

1. In this study it was found that the correlation with the maximum dose received by all the pharyngeal constrictors and mean dose to superior constrictor was significantly associated with dysphagia assessed by FEES.

2. Among the pharyngeal constrictors, superior constrictor was the one which was found to have the most significant association with dose and development of dysphagia as assessed with FEES.

3. The study also found worsening of the overall quality of life with complaints of dysphagia (assessed with the MDADI score) that correlated with findings of FEES, with statistical significance.

4. The worsening of the quality of life as reflected by MDADI score, correlated with maximum and mean doses to the pharyngeal constrictors, with statistical significance.

Longer follow up with both subjective and objective assessment is necessary to better understand the long term effect of late dysphagia in patients undergoing radiation therapy for head and neck cancers.

8. BIBLIOGRAPHY

1. Puri S, Ashat M, Pandey A, Goel NK, Singh A, Kaushal V. Socio-demographic characteristics of cancer patients: hospital based cancer registry in a tertiary care hospital of India. Indian J Cancer. 2014 Mar;51(1):1–4.

2. Bhide SA, Newbold KL, Harrington KJ, Nutting CM. Clinical evaluation of intensity-modulated radiotherapy for head and neck cancers. Br J Radiol. 2012 May;85(1013):487–94.

3. Grégoire V, De Neve W, Eisbruch A, Lee N, Van den Weyngaert D, Van Gestel D. Intensity-modulated radiation therapy for head and neck carcinoma. The Oncologist. 2007 May;12(5):555–64.

4. Chaturvedi AK, Anderson WF, Lortet-Tieulent J, Curado MP, Ferlay J, Franceschi S, et al. Worldwide trends in incidence rates for oral cavity and oropharyngeal cancers. J Clin Oncol Off J Am Soc Clin Oncol. 2013 Dec 20;31(36):4550–9.

5. Simard EP, Torre LA, Jemal A. International trends in head and neck cancer incidence rates: differences by country, sex and anatomic site. Oral Oncol. 2014 May;50(5):387–403.

6. Sharma J, Barman D, Sarma M, Sharma A, Kalita M, Kataki A, et al. Burden of head and neck cancers in Kamrup urban district cancer registry of Assam, India: a retrospective study. Int J Res Med Sci. 2014;2(4):1382.

7. Graham S, Dayal H, Rohrer T, Swanson M, Sultz H, Shedd D, et al. Dentition, diet, tobacco, and alcohol in the epidemiology of oral cancer. J Natl Cancer Inst. 1977 Dec;59(6):1611–8.

8. Chin D, Boyle GM, Porceddu S, Theile DR, Parsons PG, Coman WB. Head and neck cancer: past, present and future. Expert Rev Anticancer Ther. 2006 Jul;6(7):1111–8.

9. Muttagi SS, Chaturvedi P, Gaikwad R, Singh B, Pawar P. Head and neck squamous cell carcinoma in chronic areca nut chewing Indian women: Case series and review of literature. Indian J Med Paediatr Oncol Off J Indian Soc Med Paediatr Oncol. 2012 Jan;33(1):32–5.

10. Dayal PK, Mani NJ, Bhargava K. Prevalence of oral cancer and precancerous lesions in “pan”/’supari’ chewers. Indian J Public Health. 1978 Sep;22(3):234–45.

11. Gupta PC, Warnakulasuriya S. Global epidemiology of areca nut usage. Addict Biol. 2002 Jan;7(1):77–83.

12. Van Oijen MG, Slootweg PJ. Oral field cancerization: carcinogen-induced independent events or micrometastatic deposits? Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2000 Mar;9(3):249–56.

13. Gupta PC, Sinor PN, Bhonsle RB, Pawar VS, Mehta HC. Oral submucous fibrosis in India: a new epidemic? Natl Med J India. 1998 Jun;11(3):113–6.

14. Pfister DG, Fury MG. New Chapter in Our Understanding of Human Papillomavirus-Related Head and Neck Cancer. J Clin Oncol. 2014 Oct 20;32(30):3349–52.

15. Potentially HPV related head and neck cancers [Internet]. [cited 2015 Sep 17]. Available from: http://www.ncin.org.uk/publications/data_briefings/potentially_hpv_related_head_and_neck_cancers

16. Chu EA, Wu JM, Tunkel DE, Ishman SL. Nasopharyngeal Carcinoma: The Role of the Epstein-Barr Virus. Medscape J Med. 2008 Jul 16;10(7):165.

17. Breda E, Catarino RJF, Azevedo I, Lobão M, Monteiro E, Medeiros R. Epstein-Barr virus detection in nasopharyngeal carcinoma: implications in a low-risk area. Braz J Otorhinolaryngol. 2010 Jun;76(3):310–5.

18. Wu H-C, Lin Y-J, Lee J-J, Liu Y-J, Liang S-T, Peng Y, et al. Functional Analysis of EBV in Nasopharyngeal Carcinoma Cells. Lab Invest. 2003 Jun 1;83(6):797–812.

19. Chen M, Yin L, Wu J, Gu J-J, Jiang X-S, Wang D-J, et al. Impact of Plasma Epstein-Barr Virus-DNA and Tumor Volume on Prognosis of Locally Advanced Nasopharyngeal Carcinoma, Impact of Plasma Epstein-Barr Virus-DNA and Tumor Volume on Prognosis of Locally Advanced Nasopharyngeal Carcinoma. BioMed Res Int BioMed Res Int. 2015 Jan 31;2015, 2015:e617949.

20. Farah CS, Woo S, Zain RB, Sklavounou A, McCullough MJ, Lingen M, et al. Oral Cancer and Oral Potentially Malignant Disorders, Oral Cancer and Oral Potentially Malignant Disorders. Int J Dent Int J Dent. 2014 May 7;2014, 2014:e853479.

21. Mortazavi H, Baharvand M, Mehdipour M. Oral Potentially Malignant Disorders: An Overview of More than 20 Entities. J Dent Res Dent Clin Dent Prospects. 2014;8(1):6–14.

22. Sankaranarayanan R, Masuyer E, Swaminathan R, Ferlay J, Whelan S. Head and neck cancer: a global perspective on epidemiology and prognosis. Anticancer Res. 1998 Dec;18(6B):4779–86.

23. Reichart PA, Philipsen HP, Sciubba JJ. [The new WHO classification of tumors of the head and neck. What has changed?]. Mund- Kiefer- Gesichtschirurgie MKG. 2006 Jan;10(1):1–2.

24. Tandon S, Shahab R, Benton JI, Ghosh SK, Sheard J, Jones TM. Fine-needle aspiration cytology in a regional head and neck cancer center: comparison with a systematic review and meta-analysis. Head Neck. 2008 Sep;30(9):1246–52.

25. Pisharodi LR. False-negative diagnosis in fine-needle aspirations of squamous-cell carcinoma of head and neck. Diagn Cytopathol. 1997 Jul;17(1):70–3.

26. Ahuja AT, Ying M, Ho SY, Antonio G, Lee YP, King AD, et al. Ultrasound of malignant cervical lymph nodes. Cancer Imaging. 2008 Mar 25;8(1):48–56.

27. Vassallo P, Wernecke K, Roos N, Peters PE. Differentiation of benign from malignant superficial lymphadenopathy: the role of high-resolution US. Radiology. 1992 Apr;183(1):215–20.

28. Taha MS, Hassan O, Amir M, Taha T, Riad MA. Diffusion-weighted MRI in diagnosing thyroid cartilage invasion in laryngeal carcinoma. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2014 Sep;271(9):2511–6.

29. Becker M, Zbären P, Casselman JW, Kohler R, Dulguerov P, Becker CD. Neoplastic invasion of laryngeal cartilage: reassessment of criteria for diagnosis at MR imaging. Radiology. 2008 Nov;249(2):551–9.

30. Sobin LH, Fleming ID. TNM Classification of Malignant Tumors, fifth edition (1997). Union Internationale Contre le Cancer and the American Joint Committee on Cancer. Cancer. 1997 Nov 1;80(9):1803–4.

31. TNM staging system [Internet]. Wikipedia, the free encyclopedia. 2015 [cited 2015 Sep 25]. Available from: https://en.wikipedia.org/w/index.php?title=TNM_staging_system&oldid=675847401

32. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. 2010 Jun;17(6):1471–4.

33. Forastiere AA, Trotti A, Pfister DG, Grandis JR. Head and Neck Cancer: Recent Advances and New Standards of Care. J Clin Oncol. 2006 Jun 10;24(17):2603–5.

34. Kies MS, Bennett CL, Vokes EE. Locally advanced head and neck cancer. Curr Treat Options Oncol. 2001 Feb;2(1):7–13.

35. Varkey P, Liu Y-T, Tan NC. Multidisciplinary Treatment of Head and Neck Cancer. Semin Plast Surg. 2010 Aug;24(3):331–4.

36. Cooper JS, Zhang Q, Pajak TF, Forastiere AA, Jacobs J, Saxman SB, et al. Long-term follow-up of the RTOG 9501/intergroup phase III trial: postoperative concurrent radiation therapy and chemotherapy in high-risk squamous cell carcinoma of the head and neck. Int J Radiat Oncol Biol Phys. 2012 Dec 1;84(5):1198–205.

37. Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefèbvre J-L, Greiner RH, et al. Postoperative Irradiation with or without Concomitant Chemotherapy for Locally Advanced Head and Neck Cancer. N Engl J Med. 2004 May 6;350(19):1945–52.

38. Adelstein DJ, Li Y, Adams GL, Wagner H, Kish JA, Ensley JF, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2003 Jan 1;21(1):92–8.

39. Forastiere AA, Zhang Q, Weber RS, Maor MH, Goepfert H, Pajak TF, et al. Long-term results of RTOG 91-11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with locally advanced larynx cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2013 Mar 1;31(7):845–52.

40. al-Sarraf M. Clinical trials with fluorinated pyrimidines in patients with head and neck cancer. Invest New Drugs. 1989 Apr;7(1):71–81.

41. Pignon J-P, le Maître A, Maillard E, Bourhis J, MACH-NC Collaborative Group. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2009 Jul;92(1):4–14.

42. Vokes EE. Induction Chemotherapy for Head and Neck Cancer: Recent Data. The Oncologist. 2010 Oct 1;15(Supplement 3):3–7.

43. Lorch JH, Goloubeva O, Haddad RI, Cullen K, Sarlis N, Tishler R, et al. Induction chemotherapy with cisplatin and fluorouracil alone or in combination with docetaxel in locally advanced squamous-cell cancer of the head and neck: long-term results of the TAX 324 randomised phase 3 trial. Lancet Oncol. 2011 Feb;12(2):153–9.

44. Haddad RI, Posner MR. Induction Chemotherapy in Head and Neck Cancer. J Clin Oncol. 2009 Aug 10;27(23):e52–3.

45. Amrein PC, Colecchi CH, Finkelstein DM, Fabian RL. Adjuvant Chemotherapy in Advanced Head and Neck Cancer. The Oncologist. 1997 Jun 1;2(3):135–41.

46. Stell PM, Rawson NS. Adjuvant chemotherapy in head and neck cancer. Br J Cancer. 1990 May;61(5):779–87.

47. Price KAR, Cohen EE. Current treatment options for metastatic head and neck cancer. Curr Treat Options Oncol. 2012 Mar;13(1):35–46.

48. Molin Y, Fayette J. Current chemotherapies for recurrent/metastatic head and neck cancer. Anticancer Drugs. 2011 Aug;22(7):621–5.

49. Bonner JA, Harari PM, Giralt J, Azarnia N, Shin DM, Cohen RB, et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. N Engl J Med. 2006 Feb 9;354(6):567–78.

50. Sundaram S, Venkatanarayanan B, Sridharan N, Rajagopal GK. Study of Nimotuzumab With Concurrent Chemoradiation Therapy in Patients With Advanced Head-and-Neck Cancer. Int J Radiat Oncol • Biol • Phys. 2014 Feb 1;88(2):493–4.

51. Brahme A, Roos JE, Lax I. Solution of an integral equation encountered in rotation therapy. Phys Med Biol. 1982 Oct;27(10):1221–9.

52. Pauloski BR, Rademaker AW, Logemann JA, Discekici-Harris M, Mittal BB. Comparison of swallowing function after intensity-modulated radiation therapy and conventional radiotherapy for head and neck cancer. Head Neck. 2014 Jun 7;

53. Lin A, Kim HM, Terrell JE, Dawson LA, Ship JA, Eisbruch A. Quality of life after parotid-sparing IMRT for head-and-neck cancer: a prospective longitudinal study. Int J Radiat Oncol Biol Phys. 2003 Sep 1;57(1):61–70.

54. Radiation Therapy: Head and Neck Cancer [Internet]. Head & Neck Cancer Guide. [cited 2015 Sep 13]. Available from: http://www.headandneckcancerguide.org/adults/cancer-diagnosis-treatments/radiation-therapy/

55. Trotti A. Toxicity in head and neck cancer: a review of trends and issues. Int J Radiat Oncol Biol Phys. 2000 Apr 1;47(1):1–12.

56. Nutting CM, Morden JP, Harrington KJ, Urbano TG, Bhide SA, Clark C, et al. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Oncol. 2011 Feb;12(2):127–36.

57. Scarantino C, LeVeque F, Swann RS, White R, Schulsinger A, Hodson DI, et al. Effect of pilocarpine during radiation therapy: results of RTOG 97-09, a phase III randomized study in head and neck cancer patients. J Support Oncol. 2006 May;4(5):252–8.

58. Denaro N, Merlano MC, Russi EG. Dysphagia in Head and Neck Cancer Patients: Pretreatment Evaluation, Predictive Factors, and Assessment during Radio-Chemotherapy, Recommendations. Clin Exp Otorhinolaryngol. 2013 Sep;6(3):117–26.

59. Lohia S, Rajapurkar M, Nguyen SA, Sharma AK, Gillespie MB, Day TA. A comparison of outcomes using intensity-modulated radiation therapy and 3-dimensional conformal radiation therapy in treatment of oropharyngeal cancer. JAMA Otolaryngol-- Head Neck Surg. 2014 Apr;140(4):331–7.

60. Sonis ST, Eilers JP, Epstein JB, LeVeque FG, Liggett WH, Mulagha MT, et al. Validation of a new scoring system for the assessment of clinical trial research of oral mucositis induced by radiation or chemotherapy. Cancer. 1999 May 15;85(10):2103–13.

61. Logemann JA, Pauloski BR, Rademaker AW, Lazarus CL, Gaziano J, Stachowiak L, et al. Swallowing Disorders in the First Year After Radiation and Chemoradiation. Head Neck. 2008 Feb;30(2):148–58.

62. Lazarus CL, Logemann JA, Pauloski BR, Colangelo LA, Kahrilas PJ, Mittal BB, et al. Swallowing disorders in head and neck cancer patients treated with radiotherapy and adjuvant chemotherapy. The Laryngoscope. 1996 Sep;106(9 Pt 1):1157–66.

63. Matsuo K, Palmer JB. Anatomy and Physiology of Feeding and Swallowing – Normal and Abnormal. Phys Med Rehabil Clin N Am. 2008 Nov;19(4):691–707.

64. Nguyen NP, Frank C, Moltz CC, Vos P, Smith HJ, Bhamidipati PV, et al. Aspiration rate following chemoradiation for head and neck cancer: an underreported occurrence. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2006 Sep;80(3):302–6.

65. Eisbruch A, Schwartz M, Rasch C, Vineberg K, Damen E, Van As CJ, et al. Dysphagia and aspiration after chemoradiotherapy for head-and-neck cancer: which anatomic structures are affected and can they be spared by IMRT? Int J Radiat Oncol Biol Phys. 2004 Dec 1;60(5):1425–39.

66. Lee WT, Akst LM, Adelstein DJ, Saxton JP, Wood BG, Strome M, et al. Risk factors for hypopharyngeal/upper esophageal stricture formation after concurrent chemoradiation. Head Neck. 2006 Sep;28(9):808–12.

67. Eisbruch A, Lyden T, Bradford CR, Dawson LA, Haxer MJ, Miller AE, et al. Objective assessment of swallowing dysfunction and aspiration after radiation concurrent with chemotherapy for head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2002 May 1;53(1):23–8.

68. Eisbruch A. Dysphagia and aspiration following chemo-irradiation of head and neck cancer: major obstacles to intensification of therapy. Ann Oncol. 2004 Mar 1;15(3):363–4.

69. Feng FY, Kim HM, Lyden TH, Haxer MJ, Feng M, Worden FP, et al. Intensity-Modulated Radiotherapy of Head and Neck Cancer Aiming to Reduce Dysphagia: Early Dose–Effect Relationships for the Swallowing Structures. Int J Radiat Oncol. 2007 Aug;68(5):1289–98.

70. Levendag PC, Teguh DN, Voet P, van der Est H, Noever I, de Kruijf WJM, et al. Dysphagia disorders in patients with cancer of the oropharynx are significantly affected by the radiation therapy dose to the superior and middle constrictor muscle: a dose-effect relationship. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2007 Oct;85(1):64–73.

71. Mazzola R, Ricchetti F, Fiorentino A, Fersino S, Giaj Levra N, Naccarato S, et al. Dose-volume-related dysphagia after constrictor muscles definition in head and neck cancer intensity-modulated radiation treatment. Br J Radiol. 2014 Dec;87(1044):20140543.

72. Popovtzer A, Cao Y, Feng FY, Eisbruch A. Anatomical changes in the pharyngeal constrictors after chemoirradiation of head and neck cancer and their dose-effect relationships: MRI-based study. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2009 Dec;93(3):510–5.

73. Steele CM, Bailey GL, Chau T, Molfenter SM, Oshalla M, Waito AA, et al. The relationship between hyoid and laryngeal displacement and swallowing impairment. Clin Otolaryngol Off J ENT-UK Off J Neth Soc Oto-Rhino-Laryngol Cervico-Facial Surg. 2011 Feb;36(1):30–6.

74. Dirix P, Abbeel S, Vanstraelen B, Hermans R, Nuyts S. Dysphagia after chemoradiotherapy for head-and-neck squamous cell carcinoma: dose-effect relationships for the swallowing structures. Int J Radiat Oncol Biol Phys. 2009 Oct 1;75(2):385–92.

75. Anderson NJ, Wada M, Schneider-Kolsky M, Rolfo M, Joon DL, Khoo V. Dose-volume response in acute dysphagia toxicity: Validating QUANTEC recommendations into clinical practice for head and neck radiotherapy. Acta Oncol Stockh Swed. 2014 Oct;53(10):1305–11.

76. Bhide SA, Gulliford S, Kazi R, El-Hariry I, Newbold K, Harrington KJ, et al. Correlation between dose to the pharyngeal constrictors and patient quality of life and late dysphagia following chemo-IMRT for head and neck cancer. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2009 Dec;93(3):539–44.

77. Murphy BA, Gilbert J. Dysphagia in Head and Neck Cancer Patients Treated With Radiation: Assessment, Sequelae, and Rehabilitation. Semin Radiat Oncol. 2009 Jan;19(1):35–42.

78. Swallowing Problems (Dysphagia) After Head and Neck Cancer [Internet]. American Speech-Language-Hearing Association. [cited 2015 Sep 24]. Available from: http://www.asha.org/public/speech/disorders/Swallowing-Problems-After-Head-and-Neck-Cancer/

79. Ringash J, Bezjak A, O'Sullivan B, Redelmeier DA. Interpreting differences in quality of life: the FACT-H&N in laryngeal cancer patients. Qual Life Res Int J Qual Life Asp Treat Care Rehabil. 2004 May;13(4):725–33.

80. Trotti A, Johnson DJ, Gwede C, Casey L, Sauder B, Cantor A, et al. Development of a head and neck companion module for the quality of life-radiation therapy instrument (QOL-RTI). Int J Radiat Oncol Biol Phys. 1998 Sep 1;42(2):257–61.

81. Bjordal K, Hammerlid E, Ahlner-Elmqvist M, Graeff A de, Boysen M, Evensen JF, et al. Quality of Life in Head and Neck Cancer Patients: Validation of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-H&N35. J Clin Oncol. 1999 Mar 1;17(3):1008–1008.

82. Carrillo JF, Ortiz-Toledo MA, Salido-Noriega Z, Romero-Ventura NB, Ochoa-Carrillo FJ, Oñate-Ocaña LF. Validation of the Mexican Spanish version of the EORTC QLQ-H&N35 instrument to measure health-related quality of life in patients with head and neck cancers. Ann Surg Oncol. 2013 May;20(5):1417–26.

83. Singer S, Wollbrück D, Wulke C, Dietz A, Klemm E, Oeken J, et al. Validation of the EORTC QLQ-C30 and EORTC QLQ-H&N35 in patients with laryngeal cancer after surgery. Head Neck. 2009 Jan;31(1):64–76.

84. Singer S, Arraras JI, Baumann I, Boehm A, Chie W-C, Galalae R, et al. Quality of life in patients with head and neck cancer receiving targeted or multimodal therapy--update of the EORTC QLQ-H&N35, Phase I. Head Neck. 2013 Sep;35(9):1331–8.

85. Chen AY, Frankowski R, Bishop-Leone J, Hebert T, Leyk S, Lewin J, et al. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the M. D. Anderson dysphagia inventory. Arch Otolaryngol Head Neck Surg. 2001 Jul;127(7):870–6.

86. Schindler A, Borghi E, Tiddia C, Ginocchio D, Felisati G, Ottaviani F. Adaptation and validation of the Italian MD Anderson Dysphagia Inventory (MDADI). Rev Laryngol - Otol - Rhinol. 2008;129(2):97–100.

87. Carrillo JF, Ortiz-Toledo MA, Salido-Noriega Z, Romero-Ventura NB, Ochoa-Carrillo FJ, Oñate-Ocaña LF. Validation of the Mexican Spanish version of the EORTC QLQ-H&N35 instrument to measure health-related quality of life in patients with head and neck cancers. Ann Surg Oncol. 2013 May;20(5):1417–26.

88. Deantonio L, Masini L, Brambilla M, Pia F, Krengli M. Dysphagia after definitive radiotherapy for head and neck cancer. Correlation of dose-volume parameters of the pharyngeal constrictor muscles. Strahlenther Onkol Organ Dtsch Röntgenges Al. 2013 Mar;189(3):230–6.

89. Carlsson S, Rydén A, Rudberg I, Bove M, Bergquist H, Finizia C. Validation of the Swedish M. D. Anderson Dysphagia Inventory (MDADI) in patients with head and neck cancer and neurologic swallowing disturbances. Dysphagia. 2012 Sep;27(3):361–9.

90. Schindler A, Borghi E, Tiddia C, Ginocchio D, Felisati G, Ottaviani F. Adaptation and validation of the Italian MD Anderson Dysphagia Inventory (MDADI). Rev Laryngol - Otol - Rhinol. 2008;129(2):97–100.

91. Langmore SE. Evaluation of oropharyngeal dysphagia: which diagnostic tool is superior? Curr Opin Otolaryngol Head Neck Surg. 2003 Dec;11(6):485–9.

92. Nacci A, Ursino F, La Vela R, Matteucci F, Mallardi V, Fattori B. Fiberoptic endoscopic evaluation of swallowing (FEES): proposal for informed consent. Acta Otorhinolaryngol Ital. 2008 Aug;28(4):206–11.

93. Hiss SG, Postma GN. Fiberoptic endoscopic evaluation of swallowing. The Laryngoscope. 2003 Aug;113(8):1386–93.

94. Kelly AM, Drinnan MJ, Leslie P. Assessing penetration and aspiration: how do videofluoroscopy and fiberoptic endoscopic evaluation of swallowing compare? The Laryngoscope. 2007 Oct;117(10):1723–7.

95. Langmore SE, Schatz K, Olson N. Endoscopic and videofluoroscopic evaluations of swallowing and aspiration. Ann Otol Rhinol Laryngol. 1991 Aug;100(8):678–81.

96. Cohen MA, Setzen M, Perlman PW, Ditkoff M, Mattucci KF, Guss J. The safety of flexible endoscopic evaluation of swallowing with sensory testing in an outpatient otolaryngology setting. The Laryngoscope. 2003 Jan;113(1):21–4.

97. Grégoire V, Ang K, Budach W, Grau C, Hamoir M, Langendijk JA, et al. Delineation of the neck node levels for head and neck tumors: a 2013 update. DAHANCA, EORTC, HKNPCSG, NCIC CTG,

NCRI, RTOG, TROG consensus guidelines. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2014 Jan;110(1):172–81.

98. Jordan K, Sippel C, Schmoll H-J. Guidelines for Antiemetic Treatment of Chemotherapy-Induced Nausea and Vomiting: Past, Present, and Future Recommendations. The Oncologist. 2007 Sep 1;12(9):1143–50.

99. Van der Laan HP, Bijl HP, Steenbakkers RJHM, van der Schaaf A, Chouvalova O, Vemer-van den Hoek JGM, et al. Acute symptoms during the course of head and neck radiotherapy or chemoradiation are strong predictors of late dysphagia. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2015 Apr;115(1):56–62.

9. ANNEXURES

INFORMATION SHEET AND CONSENT FORM

Christian Medical College, Vellore
Department of Radiation therapy
Patient's Information sheet

Association between the radiation dose to the pharyngeal constrictors and swallowing dysfunction and patients' quality of life following chemo irradiation for head and neck cancers

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You are being requested to participate in a study which aims to find an association between the radiation dose delivered to the pharyngeal constrictor muscles and its effect on the swallowing capability in patients of head and neck cancer undergoing treatment with radical chemo irradiation.

What does this study do?

This is an observational study to assess the quality of life and swallowing difficulty in patients diagnosed to have head and neck cancer undergoing treatment with radiation therapy and chemotherapy. It has been seen that patients develop difficulty in swallowing during the course of radiation therapy which significantly affects their quality of life.

In this observational study, we would like to assess patients' quality of life by using simple questionnaires and endoscopy procedures and then evaluate the effect of swallowing difficulty in these patients due to the dose of radiation therapy delivered to the muscles helping in swallowing.

This will help us in the future by reducing dose to these muscles helpful in swallowing and will thus help in improving patients' quality of life

Does this study have any side effects?

This is an observational study with no particular side effects.

If you take part what will you have to do?

If you agree to participate in this study, you will be given a dysphagia score questionnaire form to be filled up before your treatment, during the middle of your treatment and also in the subsequent routine follow up visits at 6 weeks and 3 months. You will also have to undergo an endoscopic evaluation of your swallowing ability of liquids and solids, along with the filling up of the questionnaire.

All other treatments that you are already on will be continued and your regular treatment will not be changed during this study. One additional endoscopy will be done for the evaluation of your swallowing capability during the course of the treatment and you will not have to pay for that endoscopic procedure.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

Since this is an observational study, no particular study related side effects are expected. However, during the course of endoscopy for the evaluation of dysphagia, you may experience some pain or uneasiness.

Will you have to pay for the study?

This is an observational study and there is no change in the standard treatment of care. You need not pay anything more than the regular treatment charges as applicable for the radiation therapy and the chemotherapy.

What happens after the study is over?

You will be advised to have regular checkups at the specified intervals as advised which will be every 3 months in the first one year, every six months for the next two years and yearly thereafter.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission.

INFORMED CONSENT FORM

A study to find the association between the radiation dose to the pharyngeal constrictors and swallowing dysfunction and patients' quality of life following chemo irradiation for head and neck cancers

Subject's Initials: _____

Subject's Name: _____

Date of Birth / Age: _____

For illiterate subjects : As read to me

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

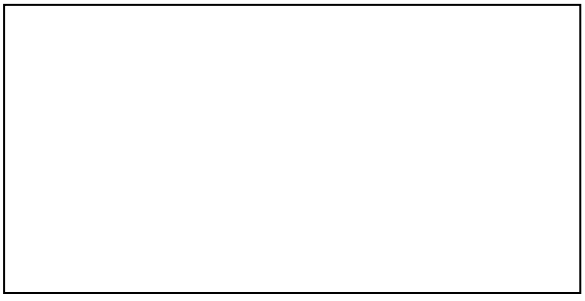
(v) I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____ Signature:

Or



Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

Association between the radiation dose to the pharyngeal constrictors and swallowing dysfunction and patients' quality of life following chemo irradiation for head and neck cancers

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FEES ASSESSMENT REPORT

Patient Name:
Hospital Number:
Date of Birth /age
Date of Assessment:

Diagnosis:

Other relevant Medical / Surgical History:

ASSESSMENT INFORMATION

A NASOPHARYNX COMMENTS
Anatomy WNL / ONL _____
Symmetry of Closure WNL / ONL _____
Degree of closure WNL / ONL _____
Closure pattern Circular / Coronal _____

B BASE OF TONGUE
Anatomy WNL / ONL _____
Symmetry of movement WNL / ONL _____
Range of movement WNL / ONL _____

C HYPOPHARYNX
Anatomy WNL / ONL _____
Symmetry WNL / ONL _____
Range of movement WNL / ONL _____

D LARYNX
Anatomy WNL / ONL _____
Symmetry at rest WNL / ONL _____
Symmetry of closure & phonation WNL / ONL _____

E AIRWAY PROTECTION *(Murray 1999)*
Breath holding not achieved
Transient breath holding with glottis open
Sustained breath holding with glottis open
Transient true fold closure
Sustained true fold closure
Transient true and ventricular fold closure
Sustained true and ventricular fold closure
Vocal fold closure on voluntary cough

F SECRETION RATING *(Murray 1999)*
O Normal rating: ranges from no visible secretions anywhere in the hypopharynx, to some transient secretions visible in the valleculae and pyriform sinuses. These secretions are not bilateral or deeply pooled.
1 Any secretions evident upon entry or following a dry swallow in the protective structures surrounding the laryngeal vestibule that are bilaterally represented or deeply pooled. This rating would include cases in which there is transition in the accumulation of secretions during observation segment.
2 Any secretions that change from "1"" to a "3" rating during the observation period.
3 Most severe rating. Any secretions seen in the area defined as laryngeal vestibule. Pulmonary secretions are included if they are not cleared by swallowing or coughing by the close of the segment.

G PENETRATION – ASPIRATION SCALE *(Rosenbek 1996)*
1 Material does not enter the airway
2 Material enters the airway, remains above the vocal folds and is ejected from the airway
3 Material enters the airway, remains above the vocal folds, and is not ejected from the airway
4 Material enters the airway, contacts the vocal folds, and is ejected from the airway
5 Material enters the airway, contacts the vocal folds, and is not ejected from the airway
6 Material enters the airway, passes below the vocal folds, and is ejected into the larynx or out of the airway
7 Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort
8 Material enters the airway, passes below the vocal folds, and no effort is made to eject

Consistencies Outcome

Thin syrup (liquid)
_____
Thick cerelac
(semisolid)_____

COMMENTS

Association between the radiation dose to the pharyngeal constrictors and swallowing dysfunction and patients' quality of life following chemo irradiation for head and neck cancers

This questionnaire asks for your views about your swallowing ability. This Information will help us understand how you feel about swallowing.

The following statements have been made by people who have problems with their swallowing. Some of the statements may apply to you.

Please read each statement and circle the response which best reflects your experience in the past week.

1. My swallowing ability limits my day-to-day activities
Strongly Agree Agree No Opinion Disagree Strongly Disagree

2. I am embarrassed by my eating habits
Strongly Agree Agree No Opinion Disagree Strongly Disagree

3. People have difficulty cooking for me
Strongly Agree Agree No Opinion Disagree Strongly Disagree

4. Swallowing is more difficult at the end of the day
Strongly Agree Agree No Opinion Disagree Strongly Disagree

5. I do not feel self-conscious when I eat
Strongly Agree Agree No Opinion Disagree Strongly Disagree

6. I am upset by my swallowing problem
Strongly Agree Agree No Opinion Disagree Strongly Disagree

7. Swallowing takes great effort
Strongly Agree Agree No Opinion Disagree Strongly Disagree

8. I do not go out because of my swallowing problem
Strongly Agree Agree No Opinion Disagree Strongly Disagree

9. My swallowing difficulty has caused me to lose income
Strongly Agree Agree No Opinion Disagree Strongly Disagree

10. It takes me longer to eat because of my swallowing problem
Strongly Agree Agree No Opinion Disagree Strongly Disagree

11. People ask me “Why can’t you eat that?”
Strongly Agree Agree No Opinion Disagree Strongly Disagree

12. Other people are irritated by my eating problem
Strongly Agree Agree No Opinion Disagree Strongly Disagree

13. I cough when I try to drink liquids
Strongly Agree Agree No Opinion Disagree Strongly Disagree

14. My swallowing problems limit my social and personal life
Strongly Agree Agree No Opinion Disagree Strongly Disagree

15. I feel free to go out to eat with my friends, neighbors and relatives
Strongly Agree Agree No Opinion Disagree Strongly Disagree

16. I limit my food intake because of my swallowing difficulty
Strongly Agree Agree No Opinion Disagree Strongly Disagree

17. I cannot maintain my weight because of my swallowing problem
Strongly Agree Agree No Opinion Disagree Strongly Disagree

18. I have low self-esteem because of my swallowing problem
Strongly Agree Agree No Opinion Disagree Strongly Disagree

19. I feel that I am swallowing a huge amount of food
Strongly Agree Agree No Opinion Disagree Strongly Disagree

20. I feel excluded because of my eating habits
Strongly Agree Agree No Opinion Disagree Strongly Disagree

CHRISTIAN MEDICAL COLLEGE, VELLORE
DEPARTMENT OF RADIOTHERAPY UNIT II
SYSTEMIC THERAPY
PATIENT INFORMATION AND CONSENT FORM

I _____ Hospital No_____ son/daughter/wife of _____ aged _____resident of door No _____ Street,_____ Town, _____ District, _____ State, being under the treatment in Radiotherapy Department Unit 2 of Christian Medical College, Vellore, do hereby give consent to receive

- ☐ Primary Chemotherapy
- ☐ Neoadjuvant chemotherapy
- ☐ Concurrent chemotherapy
- ☐ Adjuvant chemotherapy
- ☐ Palliative chemotherapy
- ☐ Hormonal agent treatment
- ☐ Biological agent treatment

for _____ (diagnosis, histology and stage)

I have been informed by Dr_____ that the above therapy is recommended for this condition. I have been explained about the various possible treatment modalities available and their benefits, risks and outcome. I have understood the risks, benefits and outcome of the various treatment options explained to me and have opted for the above treatment.

I understand that the aim of my treatment is

- ☐ Curative: Try to give the best possible chance of cure
- ☐ Palliative: Try to reduce/control the symptoms

Try to improve my quality of life

I understand that the medications recommended by my doctor can have short-term and long-term side effects. My doctor talked to me about the following side effects that I might experience because of the above mentioned medications.

- ☐ Nausea /Vomiting _____
- ☐ Hair Loss_____
- ☐ Low red blood cell count/Anemia_____
- ☐ Fatigue/Tiredness/Asthenia_____
- ☐ Sores of Mouth and Throat (Mucositis)____
- ☐ Muscle/Bone _____
- ☐ Nerve _____
- ☐ Sexual _____
- ☐ Reproductive/Fertility _____
- ☐ Risk of Infection (due to low blood counts)_
- ☐ Risk of Bleeding (due to low platelet counts)
- ☐ Constipation_____
- ☐ Diarrhea _____
- ☐ Kidney/Bladder _____
- ☐ Heart _____
- ☐ Lung _____
- ☐ Hearing and Visual _____
- ☐ Skin _____
- ☐ Other_____

CHRISTIAN MEDICAL COLLEGE, VELLORE
DEPARTMENT OF RADIOTHERAPY UNIT II
SYSTEMIC THERAPY
PATIENT INFORMATION AND CONSENT FORM

I understand that I could even have some side effects that are above that are not listed in this form. Each patient can respond differently to medications and I could have side effects that have not been reported by others. To some extent, the side effects are reversible on stopping the medications.

I understand that any procedure in addition to the treatment described in this form will only be carried out if it is necessary and in my best interest and can be justified for medical reasons.

I understand that the treatment may be carried out by any one of the team members of the department of Radiotherapy.

I was also informed about the cost which I am expected to pay for the above treatment is as per the schedule of rates approved by the management of CMC Vellore.

I agree that my treatment details can be used for teaching and research purposes that could benefit other patients. I understand that all research work will be undertaken in accordance with appropriate ethical, legal and professional standards.

For females only: I declare that I am not pregnant now and have no reason to suspect I am pregnant. I understand if I become pregnant during the treatment my baby may be harmed hence I shall reveal the same to the doctors at once failing which I will be responsible for all the consequences. Doctor advised me to discuss about the pregnancy issues to avoid teratogenic effects of the above treatment

I have read this consent form. It has been fully explained to me in _____ language which I can understand/read and write on _____. I acknowledge that this information is not a guarantee concerning the results of chemotherapy/Hormonal therapy/Biological therapy. I voluntarily accept this treatment and the risks associated with it. I have signed the consent out of my free will without any pressure and in my full senses. I have been given the choice to withdraw myself from the treatment whenever I want to do so.

I declare that I am more than 18 years of age, hence legally entitled for giving this consent.

Signature of the patient	Signature of the doctor
Name	Name and Registration No
Place	Place
Date	Date
Time	Time
Witness 1._____	Witness 2._____
Signature	Signature
Name in Capital	Name in capital
Residential address	Residential address

CHRISTIAN MEDICAL COLLEGE, VELLORE
DEPARTMENT OF RADIOTHERAPY UNIT II
EXTERNAL RADIOTHERAPY
PATIENT INFORMATION AND CONSENT FORM

For the special radiotherapy techniques (3DCRT, IMRT, SRT) the radiotherapy planning process will take about 5-10 days time before starting the treatment. I also understand that the radiotherapy machine may go out of order and may take several days for repair. During this period radiation may have to be suspended or I may be treated in another machine if possible.

I understand that any procedure in addition to the treatment described in this form will only be carried out if it is necessary and in my best interest and can be justified for medical reasons.

I understand that the treatment may be carried out by any one of a team of members of the department of Radiotherapy.

I was also informed about the cost which I am expected to pay for the above treatment is as per the schedule of rates approved by the management of CMC Vellore.

I agree that my treatment details can be used for teaching and research purposes that could benefit other patients. I understand that all research work will be undertaken in accordance with appropriate ethical, legal and professional standards.

For females only: I declare that I am not pregnant now and have no reason to suspect I am pregnant. I understand if I become pregnant during the treatment my baby may be harmed hence I shall reveal the same to the doctors at once failing which I will be responsible for all the consequences.

I have read this consent form. This consent form has been fully explained to me in_____ which I can understand/read and write on _____. I acknowledge that this information is not a guarantee concerning the results of radiotherapy. I voluntarily accept this treatment and the risks associated with it. I have signed the consent out of my free will without any pressure and in my full senses. I have been given the choice to withdraw myself from the treatment whenever I want to do so.

I declare that I am more than 18 years of age hence legally entitled for giving this consent.

Signature of the patient	Signature of the doctor
Name	Name and Registration No
Place	Place
Date &Time	Date &Time
Witness 1._____	Witness 2._____
Signature	Signature
Name in Capital	Name in capital
Residential address	Residential address

CHRISTIAN MEDICAL COLLEGE, VELLORE
DEPARTMENT OF RADIOTHERAPY UNIT II
EXTERNAL RADIOTHERAPY
PATIENT INFORMATION AND CONSENT FORM

I _____ Hospital No_____ son / daughter / wife of _____ aged ____resident of Door No _____ Street, _____ Town, _____ District, _____ State, being under the treatment in Radiotherapy Department Unit 2 of Christian Medical College, Vellore, do hereby give consent to undergo

- ☐ Conventional radiotherapy
- ☐ 3 Dimensional Conformal radiotherapy (3DCRT) with 2D/3D image verification
- ☐ Intensity Modulated Radiotherapy (IMRT) with 2D/3D image verification
- ☐ Stereotactic Radiotherapy (SRT)
- ☐ Total Body Irradiation (TBI)/Total Skin Electron Therapy (TSET)
- ☐ Palliative radiotherapy

treatment for _____ (diagnosis, histology and stage)

I have been informed by Dr_____ that radiotherapy is recommended for this condition. He / She also explained about the various possible treatment modalities available and their benefits, risks and outcome. I have understood the risks, benefits and outcome of the various treatment options explained to me and have opted for the above treatment.

I understand that the aim of my treatment is

- ☐ Curative: Try to give the best possible chance of cure
- ☐. Palliative: Try to reduce/control the symptoms ;

  Try to improve my quality of life

I have been explained about the early side effects which usually occur within days or weeks of starting treatment and resolve within weeks of its completion as well as about the late side effects which are uncommon, may occur months or years after the treatment completion.

Early side effects may include: _____

_____

Late side effects may include: _____

_____

There is a very small risk of developing a second cancer at some time in the future as a result of receiving radiotherapy also explained to me.

I agree to the use of permanent skin marks(Tattoos), for the purpose of accurate treatment

CHRISTIAN MEDICAL COLLEGE, VELLORE.

Dr Ida B Scudder Cancer Centre
Department of Radiation Therapy unit II

HEAD AND NECK - P R O F O R M A

Name: Hosp.No. R.T. No.
Age : DOB: Sex:
Address:
Local Permanent

Ph no Ph no

Socioeconomic status: 1. Patient's Occupation :
2. Patient's Education :

Presenting complaints:

	Y/N	Duration
Throat pain		
Dysphagia(liquids/semisolids/solids)		
Hoarseness		
Cough		
Stridor		
Neck swelling:		
Headache :		
Others:		

Addictions:

1. Smoking Y/N Number per day- Duration - /yrs
2. Smokless Tobacco Y/N Duration - /yrs
   Type:
3. Alcohol Y/N Amount & frequency - Duration - /yrs

Associated diseases: Premalignant conditions
DM/ HT/ TB/ Others
Allergies

Past history: Previous malignancies
Surgeries
major illness

Drug history:

Treatment History: Surgery(Elsewhere/ At CMCH)-
Radiotherapy(Elsewhere/ At CMCH)-
Chemotherapy(Elsewhere/ At CMCH)-

Family history-

GENERAL EXAMINATIONS:

Performance status: ECOG
Physical parameters :Weight- Height- BSA-
Vitals :BP- PR-
Pallor/ Icterus/ Edema
Stridor / Tracheostomy / Ryles tube
Systemic examination: CVS
RS
Abdomen

Local examination:

NPL scopy /IDL Sopy

Neck-
Lymphnodes-Y/N

Side	Level	no	Size	Mobile/ Fixed	Discrete/ Matted	Skin –Free/ Tethered Ulcerated
right	1					
	2					
	3					
	4					
	5					
left	1					
	2					
	3					
	4					
	5					

Clinical Diagnosis:

Site: **T N M** **Stage:**

DATA

FEES DATA

PRE-S-P1	PRE-S-P2	PRE-S-P3	PRE-S-P4	MID-S-P1	MID-S-P2	MID-S-P3	MID-S-P4	END-S-P1	END-S-P2	END-S-P3	END-S-P4	RYLES TUBE
0	1	0	0	0	1	0	0	0	1	0	0	0
0	1	0	0	0	1	0	0	0	1	0	0	0
0	1	0	0	0	1	0	0	0	1	0	0	0
0	1	1	1	0	1	1	1	1	1	2	2	1
0	1	0	0	0	1	1	1	0	1	1	1	0
0	1	0	0	1	1	1	0	1	1	1	1	0
0	1	0	0	1	1	2	2	1	1	2	2	1
0	1	0	0	1	1	1	1	2	2	2	2	1
0	1	0	0	0	1	2	2	1	1	2	2	0
0	1	0	0	1	1	1	1	2	1	2	2	1
0	1	0	0	1	1	0	0	1	1	2	1	1
0	1	1	1	1	1	1	1	2	1	2	2	1
0	1	0	0	1	1	1	1	1	1	1	2	0
0	1	0	1	0	1	1	1	1	1	2	2	0

MDADI DATA

PRE-Q-TOTAL	PRE-Q-GLC	PRE-Q-EMP	PRE-Q-FUN	PRE-Q-PHYSI	PRE-Q-P6	PRE-Q-F	PRE-Q-P8	MID-Q-TOT	MID-Q-GLOBA	MID-Q-EMOT	MID-Q-FUNCTI	MID-Q-PHY	MID-Q-P6	MID-Q-P7	MID-Q-P8	END-Q-TOTAL	END-Q-GLOI	END-Q-EMOTI	END-Q-FUNC	END-Q-PHYSI	END-Q-P6	END-Q-P7	END-Q-P8
100	5	30	25	40	5	5	5	74	5	26	15	28	4	5	2	74	4	24	21	25	4	4	4
100	5	30	25	40	5	5	5	100	5	30	25	40	5	5	5	82	4	25	19	34	4	4	4
70	4	22	20	24	4	2	2	70	2	22	20	26	4	2	4	66	2	20	23	21	2	2	4
81	4	26	17	34	4	5	5	38	2	12	10	14	2	1	2	42	2	12	13	16	2	1	2
100	5	30	25	40	5	5	5	86	4	26	23	33	4	4	4	75	4	24	19	28	2	2	4
100	5	30	25	40	5	5	5	82	4	25	21	32	4	4	4	48	2	16	13	17	2	2	2
100	5	30	25	40	5	5	5	75	4	21	20	30	4	2	4	74	4	21	20	29	2	3	4
94	5	29	24	36	5	5	5	66	4	20	18	24	2	2	4	45	2	14	11	18	2	2	3
65	5	19	13	28	4	1	4	53	1	13	18	21	4	1	4	58	1	15	21	21	1	1	4
98	5	30	24	39	5	5	5	50	4	17	12	17	2	2	1	46	2	16	13	15	2	2	2
100	5	30	25	40	5	5	5	65	4	19	17	25	2	2	4	50	4	13	15	18	2	2	2
96	5	30	25	36	4	2	5	60	2	21	15	22	2	2	4	44	2	12	14	16	1	1	4
86	4	25	22	35	4	4	4	53	2	16	15	20	2	2	2	50	2	16	15	17	2	2	3
100	5	30	25	40	5	5	5	80	5	25	20	30	4	4	5	58	3	15	20	20	2	2	3

DOSIMETRY

a.

SC-V10	SC-V20	SC-V30	SC-V40	SC-V45	SC-V50	SC-V55	SC-V60	SC-V65	SC-V70	MC-V10	MC-V20	MC-V30	MC-V40	MC-V45	MC-V50	MC-V55	MC-V60	MC-V65	MC-V70
100	100	100	100	100	100	100	100	98	0	100	100	100	100	100	100	96	82	68	2
100	100	100	70	26	5	1	0	0	0	100	100	100	34	0.3	0	0	0	0	0
100	100	100	100	100	100	100	99	0	0	100	100	100	100	100	100	98	79	0	0
100	100	100	100	99	78	45	28	0	0	100	100	100	100	100	100	97	61	0	0
100	100	100	93	84	56	1	0	0	0	100	100	100	100	100	40	1.3	0	0	0
100	100	100	100	100	95	81	14	0	0	100	100	100	100	100	99	51	0	0	0
100	100	100	100	100	100	100	100	6	0	100	100	100	100	100	100	100	97	10	0
100	100	100	100	100	100	88	77	75	69	100	100	100	100	100	100	100	100	100	100
100	100	100	100	100	94	87	74	62	0.6	100	100	100	99	91	83	72	62	52	1.4
100	100	100	100	100	82	34	13	0	0	100	100	100	100	100	56	4.8	0	0	0
100	100	100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	96	84	60
100	100	100	100	100	100	100	100	100	98	100	100	100	100	100	100	100	89	69	25
100	100	100	100	96	84	62	20	0	0	100	100	100	100	100	100	56	5.6	0	0
93	88	82	68	53	34	28	24	18	8	100	100	100	100	100	100	100	100	100	97

b.

IC-V10	IC-V20	IC-V30	IC-V40	IC-V45	IC-V50	IC-V55	IC-V60	IC-V65	IC-V70	TC-V10	TC-V20	TC-V30	TC-V40	TC-V45	TC-V50	TC-V55	TC-V60	TC-V65	TC-V70
100	100	100	100	100	88	39	11	3	0	100	100	100	100	100	96	83	72	67	1
100	100	100	9	0	0	0	0	0	0	100	100	100	49	14	3	0	0	0	0
100	100	100	100	100	74	11	0	0	0	100	100	100	100	100	91	71	63	0	0
100	100	100	100	74	41	28	18	0	0	100	100	100	100	91	70	48	30	0	0
100	100	100	100	56	12	0	0	0	0	100	100	100	96	82	43	1.5	0	0	0
100	100	95	30	12	3	0.7	0	0	0	100	100	98	79	12	3.7	0.6	0	0	0
100	100	100	100	100	100	100	98	9.7	0	100	100	100	100	100	100	100	99	24	0
100	100	100	100	100	100	80	54	44	32	100	100	100	100	100	100	88	78	74	69
100	100	55	34	25	15	9.2	4.8	0.6	0	100	100	88	82	78	71	62	53	43	0.5
100	100	100	100	98	66	18	0	0	0	100	100	100	100	98	65	17	0	0	0
100	100	100	100	100	100	100	47	29	15	100	100	100	100	100	96	99	84	77	70
100	100	100	100	100	100	50	15	4.7	0.1	100	100	100	100	100	100	88	77	71	62
100	100	100	100	100	100	30	6	0	0	100	100	100	100	98	92	51	12	0	0
100	100	100	100	100	100	100	100	100	90	96	94	91	84	77	68	65	63	60	51

c.

SC-VOL	MC-VOL	IC-VOL	TC-VOL	SC-MIN	SC-MAX	SC-MEAN	MC-MIN	MC-MAX	MC-MEAN	IC-MIN	IC-MAX	IC-MEAN	TC-MIN	TC-MAX	TC-MEAN
4.9	1.6	2.3	9.3	64	70	67	0	70	65	0	68	54	0	70	63
6.7	2	2.6	12	34	48	41	34	48	39	34	46	39	34	48	39
4.8	1.2	2.8	9.3	59	63	61	52	64	61	47	61	51	47	64	58
3.4	0.6	2.2	6.6	45	62	55	52	62	59	41	62	50	41	62	54
6.2	2.2	2.5	11.6	29	57	49	45	55	49	41	55	46	29	57	48
4.4	1.9	2.8	9.6	45	62	56	49	60	54	26	56	37	26	62	50
2.8	1.1	2.6	7.5	59	66	63	59	66	63	60	68	64	59	68	63
2.7	2.2	2.2	7.4	49	74	67	70	74	72	50	74	63	49	74	68
2.8	0.8	1.4	5.4	43	70	63	38	70	61	20	66	35	20	70	55
3.8	2	1.4	7.9	46	62	53	44	60	50	42	58	51	42	62	52
5	1.1	2.4	9	69	73	71	56	72	69	54	72	61	54	73	68
7.2	2	2.8	12	69	74	72	56	72	66	50	70	56	50	74	67
4.4	1.4	3	9.4	34	53	45	41	50	45	40	49	44	0	53	45
5	1.8	3	10.4	50	71	45	69	72	71	69	72	70	50	72	58